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Requestor's Name: Delacroix

Serial Number: 09/049,227

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1803

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Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).

Please search the following:

(I) a pharmaceutical composition comprising fluoxetine or enantiomers thereof, wherein the composition is substantially free of lactose.

(IV) also please search anhydrous or non-hygroscopic compositions containing fluoxetine that may contain lactose, in addition to other known pharmaceutical excipients.

fluoxetine = Prozac

Redmond Butler Wald

See attached

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Type of Search
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- A.A. Sequence
- Structure
- Bibliographic

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- ✓ STN
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- APS
- Geninfo
- SDC
- DARC/Questel
- Other

PTO-1590 (9-90)

Delacroix
09/049227

- key terms
Fluoxetine
Query 1

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     FILE 'REGISTRY' ENTERED AT 13:44:15 ON 15 DEC 1998
L1             2 SEA ABB=ON  PLU=ON  (56296-78-7 OR 54910-89-3)/RN
                 E LACTOSE/CN 5
L2             1 SEA ABB=ON  PLU=ON  LACTOSE/CN

     FILE 'CAPLUS' ENTERED AT 13:44:55 ON 15 DEC 1998
           S 56296-78-7/REG# OR  54910-89-3/REG# OR L1 OR FLUOXETINE
    FILE 'REGISTRY' ENTERED AT 13:45:17 ON 15 DEC 1998
L3             1 SEA ABB=ON  PLU=ON  54910-89-3/RN

     FILE 'CAPLUS' ENTERED AT 13:45:17 ON 15 DEC 1998
L4          1313 SEA ABB=ON  PLU=ON  L3

     FILE 'REGISTRY' ENTERED AT 13:45:19 ON 15 DEC 1998
L5             1 SEA ABB=ON  PLU=ON  56296-78-7/RN

     FILE 'CAPLUS' ENTERED AT 13:45:20 ON 15 DEC 1998
L6           123 SEA ABB=ON  PLU=ON  L5
L7          2212 SEA ABB=ON  PLU=ON  L6 OR L4 OR L1 OR FLUOXETINE OR
                 PROZAC
L8             8 SEA ABB=ON  PLU=ON  L7 AND (L2 OR LACTOSE)

=> d 1-8 .bevstr

L8   ANSWER 1 OF 8  CAPLUS  COPYRIGHT 1998 ACS
AN   1998:402481  CAPLUS
DN   129:19676
TI   Pharmaceutical compositions for the treatment of depressive
     disorders
IN   Medjad, Nadia; Billardon, Martine
PA   UCB, S.A., Belg.
SO   Pat. Specif. (Petty) (Aust.), 15 pp.
     CODEN: AUXXDN
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   AU 686084          B3   19980129      AU 97-27539      19970626
     US 5747494         A    19980505      US 96-672920     19960628
PRAI US 96-672920      19960628
AB   A method for treating a depressive disorder comprises administering
     to a patient in need thereof a therapeutically effective amt. of a
     combination (i) hydroxyzine, an individual optical isomer thereof,
     or a pharmaceutically acceptable salt thereof and (ii) at least one
     therapeutic substance which is a serotonin uptake inhibitor, an
     individual optical isomer thereof or a pharmaceutically acceptable
     salt thereof, the therapeutically effective amt. being such that the
     depressive disorder is treated while avoiding the nervousness,
```

anxiety, agitation and sleep disorders assocd. with treatments using serotonin uptake inhibitors, and avoiding at the same time the loss of therapeutic effect obsd. when treatment with the classic assocn. of serotonin uptake inhibitors and benzodiazepines is used. A tablet contained **fluoxetine**.cntdot.HCl 10, hydroxyzine.cntdot.2HCl 25, **lactose** 200, and Mg stearate 1 mg. Antidepressive effects of the combination were demonstrated with rats.

IT **54910-89-3, Fluoxetine 56296-78-7, Fluoxetine** hydrochloride
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroxyzine and serotonin uptake inhibitor combination for treating depressive disorder with less side effects)

L8 ANSWER 2 OF 8 CAPLUS COPYRIGHT 1998 ACS
AN 1998:268331 CAPLUS
DN 128:326507
TI Pharmaceutical composition for rapid suspension in aqueous media
IN Calanchi, Massimo Maria; Marconi, Marco Giuseppe Raffaele; Mapelli, Luigi Giovanni
PA Eurand International S.P.A., Italy; Calanchi, Massimo Maria; Marconi, Marco Giuseppe Raffaele; Mapelli, Luigi Giovanni
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9817250	A1	19980430	WO 97-EP5863	19971023
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	GB 2318511	A1	19980429	GB 96-22090	19961023
	AU 9851887	A1	19980515	AU 98-51887	19971023
PRAI	GB 96-22090	19961023			
	WO 97-EP5863	19971023			

AB The invention provides a granular compn. useful as a pharmaceutical carrier which can be used for the prepn. of pharmaceutical compns. that are capable of rapid suspension in water or aq. media including saliva. The compns. may be used by addn. to a glass of water with stirring or taken directly in the mouth. The granular compn. may be

prepd. by a process which comprises subjecting a mixt. of a thickening agent and a disintegrating agent to wet granulation with an aq. medium as wetting agent or dry granulation to make a novel granular product and prepg. the pharmaceutical compn. from the granular product and the drug. A water-sol. inert excipient, which may be a sugar, may be mixed with the granular product prior to mixing with the drug. Base granules were prepd. contg. Keltrol F, Ac-di-Sol, Avicel PH 200 and Explotab. These granules were mixed with Karion, aspartame and orange flavor and monodose sachets were prepd. from this mixt. and 5-aminosalicylic acid coated with Eudragit S.

IT **63-42-3, Lactose**
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pharmaceutical compn. for rapid suspension in aq. media)

IT **54910-89-3, Fluoxetine**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compn. for rapid suspension in aq. media)

L8 ANSWER 3 OF 8 CAPLUS COPYRIGHT 1998 ACS
AN 1998:26204 CAPLUS
DN 128:132529
TI Screening methods for impurities in multi-sourced **fluoxetine** hydrochloride drug substances and formulations
AU Wirth, D. D.; Olsen, B. A.; Hallenbeck, D. K.; Lake, M. E.; Gregg, S. M.; Perry, F. M.
CS Lilly Research Laboratories, Eli Lilly Co., Lafayette, IN, 47902, USA
SO Chromatographia (1997), 46(9/10), 511-523
CODEN: CHRGB7; ISSN: 0009-5893
PB Friedrich Vieweg & Sohn Verlagsgesellschaft mbH
DT Journal
LA English
AB Gradient HPLC and gas chromatog. were applied as screening methods for detn. of impurities in **fluoxetine** HCl drug substances and formulated products from multiple sources. NMR spectroscopy was also used for identification of excipients and some residual solvents. Thirty potential impurities and excipients were investigated. Several impurities were obsd. in generic products using gradient HPLC that were not detected with isocratic pharmacopeial methods for **fluoxetine** HCl. Anal. of drug substance samples and capsule formulations from many different suppliers showed a wide variation in quality which, in many cases, would go undetected using isocratic methods. The quality of the innovator's product and some generic samples was high, but many generic samples contained high levels of impurities. A new impurity, N-benzyl **fluoxetine**, was obsd. in some generic samples at levels as high as 0.9%. The gradient HPLC method was

also used for stability studies and established that generic capsules formulated with **lactose** were less stable under accelerated conditions than those formulated without **lactose**
.

IT **54910-89-3P, Fluoxetine**
RL: ANT (Analyte); BYP (Byproduct); FMU (Formation, unclassified); ANST (Analytical study); FORM (Formation, nonpreparative); PREP (Preparation)
(screening methods for impurities in **fluoxetine** HCl drug substances and formulations)

IT **56296-78-7, Fluoxetine** hydrochloride
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(screening methods for impurities in **fluoxetine** HCl drug substances and formulations)

L8 ANSWER 4 OF 8 CAPLUS COPYRIGHT 1998 ACS
AN 1997:786659 CAPLUS
DN 128:26833
TI Maillard reaction of **lactose** and **fluoxetine** hydrochloride, a secondary amine
AU Wirth, David D.; Baertschi, Steven W.; Johnson, Ross A.; Maple, Steven R.; Miller, Marybeth S.; Hallenbeck, Diana K.; Gregg, Stephen M.
CS Lilly Research Laboratories, Eli Lilly and Company, Lafayette, IN, 47905, USA
SO J. Pharm. Sci. (1998), 87(1), 31-39
CODEN: JPMSAE; ISSN: 0022-3549
PB American Chemical Society
DT Journal
LA English
OS CJACS
AB Anal. of com. available generic formulations of **fluoxetine** -HCl revealed **lactose** as the most common excipient. Such formulations are inherently less stable than formulations with starch as the diluent due to the Maillard reaction between the drug, a secondary amine hydrochloride, and **lactose**. The Amadori rearrangement product was isolated and characterized; the characterization was aided by redn. with NaBH4 and subsequent characterization of this reduced adduct. The **lactose**-**fluoxetine**-HCl reaction was examd. in aq. EtOH and in the solid state, in which factors such as water content, lubricant concn., and temp. influenced the degrdn. N-Formylfluoxetine was identified as a major product of this Maillard reaction; N-formyl compds. may be useful as markers for this drug-excipient interaction. Many characteristic volatile products of the Maillard reaction were identified by GC/MS, including furaldehyde, maltol, and 2,3-dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one. Close similarity between the degrdn. products of simple mixts. and

formulated generic products was found; however, .gtoreq.1 product decompd. at a rate nearly 10 times that predicted from the simple models. Maillard products were also identified in unstressed capsules.

IT **63-42-3, Lactose 56296-78-7,**
Fluoxetine hydrochloride
RL: RCT (Reactant)
(maillard reaction of **lactose** and **fluoxetine** hydrochloride)

L8 ANSWER 5 OF 8 CAPLUS COPYRIGHT 1998 ACS
AN 1997:433704 CAPLUS
DN 127:55916
TI Prompt-release pharmaceutical compositions
IN Santus, Giancarlo; Golzi, Roberto
PA Recordati S.A. Chemical and Pharmaceutical Company, Italy
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9718798	A1	19970529	WO 96-EP5127	19961121
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9676948	A1	19970611	AU 96-76948	19961121
EP 862421	A1	19980909	EP 96-939871	19961121
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRAI IT 95-MI2427 19951122
WO 96-EP5127 19961121

AB A prompt-release pharmaceutical compn., suitable in particular for oral use, comprises (a) a plurality of nuclei having dimensions between 50 and 500 .mu.m, selected among microcrystals of the active ingredient and microgranules contg. at least one active ingredient and at least one pharmaceutically acceptable excipient, (b) a lipidic coating comprising a lipidic material sprayed in the melted state onto the nuclei, and optionally at least one hydrophilic additive, and (c) a vehicle comprising one or more pharmaceutically acceptable excipients. The coated micronuclei can form a suspension which can be reconstituted by the patient immediately before use by simply adding the suspending phase, or formed into tablets or solid

aggregates. The active ingredient is selected among those having unpleasant palatability or taste, poor stability in the administration vehicle, and hygroscopicity. Microgranules were prepd. from a mixt. contg. micronized diltiazem.cntdot.HCl 600, micronized **lactose** 2100, and PVP 300 g and coated with melted lipid components contg. glyceryl monostearate 90, white wax 8, cetyl alc. 1, and stearyl alc. 1 %. A dissoln. test according to USP showed a fast release of diltiazem.

IT **54910-89-3, Fluoxetine**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid-coated nuclei for formulating prompt-release oral compn.)

L8 ANSWER 6 OF 8 CAPLUS COPYRIGHT 1998 ACS
AN 1996:365808 CAPLUS
DN 125:19076
TI Combination of an opioid antagonist and a selective serotonin reuptake inhibitor for treatment of alcoholism and alcohol dependence
IN Cook, Leonard
PA Du Pont Merck Pharmaceutical Company, USA
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9609047	A1	19960328	WO 95-US10987	19950907
	W: AU, BR, CA, CN, CZ, EE, FI, HU, JP, KR, LT, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, UA, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9534199	A1	19960409	AU 95-34199	19950907
	EP 782445	A1	19970709	EP 95-931014	19950907
	R: AT, BE, DE, DK, FR, GB, IE, IT				

PRAI US 94-308859 19940919
WO 95-US10987 19950907

AB The invention relates to a method of treating alcoholism and alc. dependence in a mammal comprising administering to the mammal a therapeutically effective amt. of a synergistic combination of: (i) at least one opioid antagonist, and (ii) at least one selective serotonin reuptake inhibitor. The invention also relates to compns. and kits contg. the same.

IT **54910-89-3, Fluoxetine**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of an opioid antagonist and a selective serotonin reuptake inhibitor for treatment of alcoholism and alc.

dependence)

IT **63-42-3, Lact se**
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(combination of an opioid antagonist and a selective serotonin reuptake inhibitor for treatment of alcoholism and alc. dependence)

L8 ANSWER 7 OF 8 CAPLUS COPYRIGHT 1998 ACS
AN 1996:142252 CAPLUS
DN 124:185596
TI **Fluoxetine** pharmaceutical formulations
IN Arce, Mendizabal Flavia
PA Lilly S.A., Spain
SO Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 693281	A2	19960124	EP 95-304975	19950717
	EP 693281	A3	19961030		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	ES 2082723	A1	19960316	ES 94-1593	19940720
	ES 2082723	B1	19961001		
	HU 75036	A2	19970328	HU 95-2154	19950718
	US 5747068	A	19980505	US 95-503570	19950718
	NO 9502863	A	19960122	NO 95-2863	19950719
	AU 9525098	A1	19960201	AU 95-25098	19950719
	AU 692550	B2	19980611		
	FI 9503515	A	19960121	FI 95-3515	19950720
	JP 08040884	A2	19960213	JP 95-184037	19950720
	BR 9503386	A	19960227	BR 95-3386	19950720
	ZA 9506074	A	19960514	ZA 95-6074	19950720
	CN 1123142	A	19960529	CN 95-115241	19950720
	AU 9883174	A1	19981105	AU 98-83174	19980909
PRAI	ES 94-1593	19940720			
	AU 95-25098	19950719			

AB Pharmaceutical formulations of **fluoxetine** or an acid addn. salt thereof, suitable for manufg. dispersible tablets by direct compression and comprising, in addn. to the active ingredient, the appropriate excipients and coadjuvants, selected from among disintegrants, diluents, lubricants, anti-adherents, sweeteners, flavorings and, optionally, colorants. Said formulations are suitable for manufg. dispersible tablets which disintegrate in less than three min in water at 19-21.degree.C, and are appropriate for

treatment of depression.

IT **63-42-3, Lactose 54910-89-3,**
Fluoxetine 59333-67-4, Fluoxetine
hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**fluoxetine** tablets)

L8 ANSWER 8 OF 8 CAPLUS COPYRIGHT 1998 ACS
AN 1995:579739 CAPLUS
DN 122:322641
TI Fluorimetric determination of **fluoxetine** hydrochloride
AU Atmaca, Sedaf
CS Fac. Pharmacy, Univ. Istanbul, Beyazit Istanbul, Turk.
SO Pharmazie (1995), 50(4), 300-1
CODEN: PHARAT; ISSN: 0031-7144
DT Journal
LA English
AB **Fluoxetine** (I) has been widely used for the treatment of depression in recent years. This report presents a simple, sensitive and specific fluorimetric method for the detn. of I in capsules by using 7-chloro-4-nitrobenzofurazan (NBD-Cl) as fluorescence labeling reagent. The reaction between I and NBD-Cl proceeded in alk. medium. The results of the pH study indicated that max. fluorescence was obtained at pH 8.5. The derivatization reaction was studied at different temps. and at various periods. The optimum molar ratio of reagent to I was 30. Fluorescence intensity and the position of the emission maxima were dependent on the nature of the solvent used. The deriv. had max. intensity in EtOAc and it was stable in this solvent for at least 1 wk at 4.degree. in the dark. Relative std. deviations (RSD) were <0.67%, indicating reproducibility. There was no interference from most of the common ingredients such as magnesium trisilicate, di-Me polysiloxane, magnesium stearate, **lactose**, starch and CM-cellulose.

IT **54910-89-3, Fluoxetine**
RL: ANT (Analyte); ANST (Analytical study)
(fluorimetric detn. of **fluoxetine** in capsules)

=> d his l12-

(FILE 'USPATFULL' ENTERED AT 13:46:25 ON 15 DEC 1998)
L12 5 S L7(S)(L2 OR LACTOSE)
L13 5 S L7(P)(L2 OR LACTOSE)

=> s l12 or l13

L14 5 L12 OR L13

Searcher : Shears 308-4994

=> d 1-5 bib abs

L14 ANSWER 1 OF 5 USPATFULL
AN 1998:48412 USPATFULL
TI Pharmaceutical compositions for the treatment of depressive disorders
IN Medjad, Nadia, Suresnes, France
Billardon, Martine, Suresnes, France
PA U C B S.A., Brussels, Belgium (non-U.S. corporation)
PI US 5747494 980505
AI US 96-672920 960628 (8)
DT Utility
EXNAM Primary Examiner: Ivy, C. Warren; Assistant Examiner: Aulakh, Charanjit S.
LREP Wenderoth, Lind & Ponack
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 469
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for treating a depressive disorder which comprises administering to a patient in need thereof a therapeutically effective amount of a combination of

(i) hydroxyzine, an individual optical isomer thereof, or a pharmaceutically acceptable salt thereof, and

(ii) at least one therapeutic substance which is a serotonin uptake inhibitor, an individual optical isomer thereof or a pharmaceutically acceptable salt thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 2 OF 5 USPATFULL
AN 1998:47995 USPATFULL
TI Flouxetine pharmaceutical formulations
IN Mendizabal, Flavia Arce, Madrid, Spain
PA Lilly S. A., Madrid, Spain (non-U.S. corporation)
PI US 5747068 980505
AI US 95-503570 950718 (8)
PRAI ES 94-1593 940720
DT Utility
EXNAM Primary Examiner: Rose, Shep K.
LREP Titus, Robert D.; Boone, David E.
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 923
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Pharmaceutical formulations of fluoxetine or an acid addition salt thereof, suitable for manufacturing dispersible tablets by direct compression and comprising, in addition to the active ingredient, the appropriate excipients and coadjuvants, selected from among disintegrants, diluents, lubricants, anti-adherents, sweeteners, flavorings and, optionally, colorants.

Said formulations are suitable for manufacturing dispersible tablets which disintegrate in less than three minutes in water at 19.degree. C.-21.degree. C., and are appropriate for treatment of depression.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 3 OF 5 USPATFULL
AN 97:24483 USPATFULL
TI Transdermal delivery systems for the modulated administration of drugs
IN Kochinke, Frank, San Jose, CA, United States
Pfister, William R., Union City, CA, United States
Louie, Jenny, Fremont, CA, United States
Arenson, Dan, Escondido, CA, United States
PA PP Holdings Inc., Menlo Park, CA, United States (U.S. corporation)
PI US 5613958 970325
AI US 95-469178 950606 (8)
RLI Continuation-in-part of Ser. No. US 93-60907, filed on 12 May 1993, now abandoned
DT Utility
EXNAM Primary Examiner: Weiss, John G.; Assistant Examiner: Zuttarelli, P.
LREP Townsend and Townsend and Crew
CLMN Number of Claims: 44
ECL Exemplary Claim: 1
DRWN 10 Drawing Figure(s); 10 Drawing Page(s)
LN.CNT 1505
AB A transdermal delivery system for the modulated administration of drugs is described. The drug delivery device comprises a backing; a drug reservoir containing the drug, a plasticizer-type enhancer, a solvent-type enhancer, and optionally, a gelling agent; a non-rate-controlling membrane; and an adhesive layer containing a plasticizer-type enhancer. This drug delivery system is particularly useful for the administration of tolerance-inducing drugs, for example, vasodilators, such as isosorbide dinitrate.

L14 ANSWER 4 OF 5 USPATFULL
AN 96:120921 USPATFULL
TI Method for treating migraine headaches using optically pure S(+) fluoxetine

IN Young, James W., Palo Alto, CA, United States
Barberich, Timothy J., Concord, MA, United States
PA Sepracor Inc., Marlborough, MA, United States (U.S. corporation)
PI US 5589511 961231
AI US 94-228240 940415 (8)
RLI Continuation-in-part of Ser. No. US 93-67380, filed on 26 May 1993, now abandoned And Ser. No. US 91-793036, filed on 15 Nov 1991, now abandoned which is a continuation-in-part of Ser. No. US 90-566655, filed on 13 Aug 1990, now patented, Pat. No. US 5104899 , said Ser. No. US -67380 which is a division of Ser. No. US -793036
DT Utility
EXNAM Primary Examiner: Weddington, Kevin E.
LREP Pennie & Edmonds
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 867
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods and compositions are disclosed utilizing the pure S(+) isomer of fluoxetine which is a potent antidepressant and appetite suppressant substantially free of unwanted, adverse toxic or psychological effects. In addition, methods and compositions are disclosed utilizing the pure S(+) isomer of fluoxetine which is useful in treating migraine headaches, pain, in particular chronic pain, obsessive-compulsive disorders, sexual dysfunction and memory disorders. Further, methods and compositions for treating a condition alleviated or improved by inhibition of serotonin uptake in serotonergic neurons and platelets in a human using optically pure S(+) fluoxetine are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 5 OF 5 USPATFULL
AN 90:54481 USPATFULL
TI Method for the treatment of nicotine withdrawal syndrome
IN Hapworth, William E., 250 W. 57th St., New York, NY, United States 10019
Hapworth, Mada S., 250 W. 57th St., New York, NY, United States 10019
PI US 4940585 900710
AI US 89-312954 890217 (7)
DT Utility
EXNAM Primary Examiner: Schofer, Joseph L.; Assistant Examiner: Pili-Curtis, Carmen B.
LREP Lerner, David, Littenberg, Krumholz & Mentlik
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 792
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A therapeutic method for treatment of nicotine withdrawal syndrome symptoms of a patient in need thereof by administering to the patient a therapeutic composition of a pharmaceutically acceptable carrier and fluoxetine in an amount effective to provide physiological relief from the withdrawal symptoms.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his l15-; d 1-12 bib abs

(FILE 'BIOSIS, MEDLINE, EMBASE, LIFESCI, BIOTECHDS, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, PROMT, TOXLIT, TOXLINE, DRUGU, DRUGNL, DRUGB' ENTERED AT 13:48:51 ON 15 DEC 1998)
L15 20 S L8
L16 12 DUP REM L15 (8 DUPLICATES REMOVED)

L16 ANSWER 1 OF 12 TOXLIT
AN 1998:82903 TOXLIT
DN CA-129-019676D
TI Pharmaceutical compositions for the treatment of depressive disorders.
AU Medjad N; Billardon M
SO (1998). Pat. Specif. (Petty) (Aust.) PATENT NO. 686084 01/29/1998 (UCB, S.A.).
CODEN: AUXXDN.
CY BELGIUM
DT Patent
FS CA
LA English
OS CA 129:19676
EM 199807
AB A method for treating a depressive disorder comprises administering to a patient in need thereof a therapeutically effective amt. of a combination (i) hydroxyzine, an individual optical isomer thereof, or a pharmaceutically acceptable salt thereof and (ii) at least one therapeutic substance which is a serotonin uptake inhibitor, an individual optical isomer thereof or a pharmaceutically acceptable salt thereof, the therapeutically effective amt. being such that the depressive disorder is treated while avoiding the nervousness, anxiety, agitation and sleep disorders assocd. with treatments using serotonin uptake inhibitors, and avoiding at the same time the loss of therapeutic effect obsd. when treatment with the classic assocn. of serotonin uptake inhibitors and benzodiazepines is used. A tablet contained **fluoxetine**.cntdot.HCl 10, hydroxyzine.cntdot.2HCl 25, **lactose** 200, and Mg stearate 1 mg. Antidepressive effects of the combination were demonstrated with

rats.

L16 ANSWER 2 OF 12 TOXLIT
AN 1998:78451 TOXLIT
DN CA-128-326507N
TI Pharmaceutical composition for rapid suspension in aqueous media.
AU Calanchi MM; Marconi MGR; Mapelli LG
SO (1998). PCT Int. Appl. PATENT NO. 9817250 04/30/1998 (Mapelli, Luigi Giovanni).
CODEN: PIXXD2.
CY ITALY
DT Patent
FS CA
LA English
OS CA 128:326507
EM 199806
AB The invention provides a granular compn. useful as a pharmaceutical carrier which can be used for the prepn. of pharmaceutical compns. that are capable of rapid suspension in water or aq. media including saliva. The compns. may be used by addn. to a glass of water with stirring or taken directly in the mouth. The granular compn. may be prepd. by a process which comprises subjecting a mixt. of a thickening agent and a disintegrating agent to wet granulation with an aq. medium as wetting agent or dry granulation to make a novel granular product and prepg. the pharmaceutical compn. from the granular product and the drug. A water-sol. inert excipient, which may be a sugar, may be mixed with the granular product prior to mixing with the drug. Base granules were prepd. contg. Keltrol F, Ac-di-Sol, Avicel PH 200 and Explotab. These granules were mixed with Karion, aspartame and orange flavor and monodose sachets were prepd. from this mixt. and 5-aminosalicylic acid coated with Eudragit S.

L16 ANSWER 3 OF 12 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.
AN 1998237266 EMBASE
TI Monitor: Progress and profiles.
AU Lloyd A.W.
CS A.W. Lloyd, Department of Pharmacy, University of Brighton, Cockcroft Building, Moulsecoomb, Brighton BN2 4GJ, United Kingdom. a.w.lloyd@brighton.ac.uk
SO Pharmaceutical Science and Technology Today, (1998) 1/3 (136-139).
ISSN: 1461-5347 CODEN: PSTTF8
PUI S 1461-5347(98)00028-5
CY United Kingdom
DT Journal; (Short Survey)
FS 037 Drug Literature Index
039 Pharmacy
LA English
SL English

AB Monitor provides an insight into the latest developments in pharmaceutical science and technology through brief synopses of recent presentations, publications and patents, and expert commentaries on the latest technologies. There are two sections: Progress summarizes the latest developments in pharmaceutical process technology, formulation, analytical technology, sterilization, controlled drug delivery systems and regulatory issues; Profiles offers expert commentary on emerging technologies, novel processes and strategic, organizational and logistic issues underlying pharmaceutical R.epsilon.tD.

L16 ANSWER 4 OF 12 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 1
AN 1998:97950 BIOSIS
DN PREV199800097950
TI Maillard reaction of **lactose** and **fluoxetine** hydrochloride, a secondary amine.
AU Wirth, David D. (1); Baertschi, Steven W.; Johnson, Ross A.; Maple, Steven R.; Miller, Marybeth S.; Hallenbeck, Diana K.; Gregg, Stephen M.
CS (1) Lilly Res. Lab., Eli Lilly and Co., Lafayette, IN 47905 USA
SO Journal of Pharmaceutical Sciences, (Jan., 1998) Vol. 87, No. 1, pp. 31-39.
ISSN: 0022-3549.
DT Article
LA English
AB Analysis of commercially available generic formulations of **fluoxetine** HCl revealed the presence of **lactose** as the most common excipient. We show that such formulations are inherently less stable than formulations with starch as the diluent due to the Maillard reaction between the drug, a secondary amine hydrochloride, and **lactose**. The Amadori rearrangement product was isolated and characterized; the characterization was aided by reduction with sodium borohydride and subsequent characterization of this reduced adduct. The **lactose-fluoxetine** HCl reaction was examined in aqueous ethanol and in the solid state, in which factors such as water content, lubricant concentration, and temperature were found to influence the degradation. N-Formylfluoxetine was identified as a major product of this Maillard reaction and it is proposed that N-formyl compounds be used as markers for this drug-excipient interaction since they are easy to prepare synthetically. Many characteristic volatile products of the Maillard reaction have been identified by GC/MS, including furaldehyde, maltol, and 2,3-dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one. Close similarity between the degradation products of simple mixtures and formulated generic products was found; however, at least one product decomposed at a rate nearly 10 times that predicted from the simple models. Maillard products have also been identified in unstressed capsules. The main conclusion is that drugs which are secondary amines (not just primary amines as sometimes

reported) undergo the Maillard reaction with **lactose** under pharmaceutically relevant conditions. This finding should be considered during the selection of excipients and stability protocols for drugs which are secondary amines or their salts, just as it currently is for primary amines.

L16 ANSWER 5 OF 12 TOXLIT
AN 1997:101244 TOXLIT
DN CA-127-055916Z
TI Prompt-release pharmaceutical compositions.
AU Santus G; Golzi R
SO (1997). PCT Int. Appl. PATENT NO. 9718798 05/29/1997 (Recordati S.A. Chemical and Pharmaceutical Company).
CODEN: PIXXD2.
CY ITALY
DT Patent
FS CA
LA English
OS CA 127:55916
EM 199805
AB A prompt-release pharmaceutical compn., suitable in particular for oral use, comprises (a) a plurality of nuclei having dimensions between 50 and 500 .mu.m, selected among microcrystals of the active ingredient and microgranules contg. at least one active ingredient and at least one pharmaceutically acceptable excipient, (b) a lipidic coating comprising a lipidic material sprayed in the melted state onto the nuclei, and optionally at least one hydrophilic additive, and (c) a vehicle comprising one or more pharmaceutically acceptable excipients. The coated micronuclei can form a suspension which can be reconstituted by the patient immediately before use by simply adding the suspending phase, or formed into tablets or solid aggregates. The active ingredient is selected among those having unpleasant palatability or taste, poor stability in the administration vehicle, and hygroscopicity. Microgranules were prepd. from a mixt. contg. micronized diltiazem.cntdot.HCl 600, micronized **lactose** 2100, and PVP 300 g and coated with melted lipid components contg. glyceryl monostearate 90, white wax 8, cetyl alc. 1, and stearyl alc. 1 %. A dissoln. test according to USP showed a fast release of diltiazem.

L16 ANSWER 6 OF 12 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.DUPLICATE 2
AN 97345400 EMBASE
TI Screening methods for impurities in multi-sourced **fluoxetine** hydrochloride drug substances and formulations.
AU Wirth D.D.; Olsen B.A.; Hallenbeck D.K.; Lake M.E.; Gregg S.M.; Perry F.M.
CS B.A. Olsen, Lilly Research Laboratories, Eli Lilly and Company, P.O. Box 685, Lafayette, IN 47902, United States
SO Chromatographia, (1997) 46/9-10 (511-523).

Refs: 14
ISSN: 0009-5893 CODEN: CHRGB7
CY Germany, Federal Republic of
DT Journal
FS 039 Pharmacy
037 Drug Literature Index
LA English
SL English
AB Gradient high-performance liquid chromatography (HPLC) and gas chromatography were applied as screening methods for determination of impurities in **fluoxetine** hydrochloride drug substances and formulated products from multiple sources. Nuclear magnetic resonance spectroscopy was also used for identification of excipients and some residual solvents. Thirty potential impurities and excipients were investigated. Several impurities were observed in generic products using gradient HPLC that were not detected with isocratic pharmacopeial methods for **fluoxetine** hydrochloride. Analysis of drug substance samples and capsule formulations from many different suppliers showed a wide variation in duality which, in many cases, would go undetected using isocratic methods. The quality of the innovator's product and some generic samples was high, but many generic samples contained high levels of impurities. A new impurity, N-benzyl **fluoxetine**, was observed in some generic samples at levels as high as 0.9%. The gradient HPLC method was also used for stability studies and established that generic capsules formulated with **lactose** were less stable under accelerated conditions than those formulated without **lactose**.

L16 ANSWER 7 OF 12 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 98-04932 DRUGU T P S
TI Citalopram and sertralin, new antidepressives.
AU Peruche B; Schulz M
LO Eschbon, Ger.
SO Pharm.Ztg. (142, No. 48, 42-49, 1997) 2 Fig. 1 Tab. 34 Ref.
CODEN: PHZIAP ISSN: 0031-7136
AV Arzneimittelinformationsstelle der ADBA, Carl-Mannich-Strasse 26, 65760 Eschbon, Germany.
LA German
DT Journal
FA AB; LA; CT
FS Literature
AN 98-04932 DRUGU T P S
AB The new antidepressives, citalopram HBr (CT, Cipramil) and sertralin HCl (ST, Gladem, Zofolt) are reviewed with reference to their chemical structures, activities, mechanisms of action, side-effects, pharmacokinetics, dosage schedules, and indications and contraindications for use in patients with depression. Results of clinical trials comparing the effectivenesses of CT and ST with

other antidepressive drugs are discussed briefly.

ABEX The structures of CT and ST are compared with **fluoxetine**, paroxetine, imipramine and fluvoxamine. CT is available as film-tablets containing maize starch, **lactose** -monohydrate, microcrystalline cellulose (MC), copolyvidone, 85% glycerol, croscarmellose-sodium, methylhydroxypropylcelulose, Macrogol 400 and titanium dioxide (TiO2). ST is available in film-tablets containing calcium-hydrogen phosphate, MC, magnesium stearate, hydroxypropylcellulose, poly(O-carboxymethyl)starch-sodium salt, hydroxypropylmethylcellulose, TiO2, Macrogol and Polysorbate 80. CT selectively inhibits serotonin (5HT)-reuptake, enhances the analgesic effects of opiates and has little sedative activity when given either alone or with ethanol. ST selectively inhibits 5HT-reuptake, decreases expression of cerebral norepinephrine receptors during chronic dosage, and inhibits 5HT-uptake by thrombocytes. The main side-effects of CT are nausea, somnolence, mouth dryness, increased sweating, ejaculation failure, diarrhea and tremor. The main side-effects of ST are nausea, diarrhea/soft stools, tremor, vertigo, insomnia, mouth dryness, and ejaculation problems. CT and ST are contraindicated for use with fenfluramine, sumatriptan or precursors of 5HT, and interact with MAO-inhibitors, (with a risk of serotonin-syndrome), lithium, cimetidine (CT) and alcohol (ST). Trials have compared antidepressive effects of CT or ST with amitriptyline, imipramine, clomipramine, fluvoxamine and dosulepine. Other drugs mentioned are atenolol, phenytoin haloperidol, digoxin, glibenclamide, carbamazepine and warfarin. (S67/PH)

L16 ANSWER 8 OF 12 TOXLIT
AN 1996:103263 TOXLIT
DN CA-125-019076A
TI Combination of an opioid antagonist and a selective serotonin reuptake inhibitor for treatment of alcoholism and alcohol dependence.
AU Cook L
SO (1996). PCT Int. Appl. PATENT NO. 96 09047 03/28/96 (Du Pont Merck Pharmaceutical Company).
CY United States
DT Patent
FS CA
LA English
OS CA 125:19076
EM 199607
AB The invention relates to a method of treating alcoholism and alc. dependence in a mammal comprising administering to the mammal a therapeutically effective amt. of a synergistic combination of: (i) at least one opioid antagonist, and (ii) at least one selective serotonin reuptake inhibitor. The invention also relates to compns. and kits contg. the same.

Searcher : Shears 308-4994

L16 ANSWER 9 OF 12 TOXLIT
AN 1996:64325 TOXLIT
DN CA-124-185596U
TI **Fluoxetine** pharmaceutical formulations.
AU Arce MF
SO (1996). Eur. Pat. Appl. PATENT NO. 693281 01/24/96 (Lilly S.A.).
CY Spain
DT Patent
FS CA
LA English
OS CA 124:185596
EM 199605
AB Pharmaceutical formulations of **fluoxetine** or an acid addn. salt thereof, suitable for manufg. dispersible tablets by direct compression and comprising, in addn. to the active ingredient, the appropriate excipients and coadjuvants, selected from among disintegrants, diluents, lubricants, anti-adherents, sweeteners, flavorings and, optionally, colorants. Said formulations are suitable for manufg. dispersible tablets which disintegrate in less than three min in water at 19-21.degree.C, and are appropriate for treatment of depression.

L16 ANSWER 10 OF 12 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.
AN 97005336 EMBASE
TI **Fluoxetine** treatment seems to reduce the beneficial effects of cognitive-behavioral therapy in type B alcoholics.
AU Kranzler H.R.; Burleson J.A.; Brown J.; Babor T.F.
CS United States
SO Alcoholism: Clinical and Experimental Research, (1996) 20/9 (1534-1541).
Refs: 55
ISSN: 0145-6008 CODEN: ACRSDM
CY United States
DT Journal
FS 019 Rehabilitation and Physical Medicine
032 Psychiatry
040 Drug Dependence, Alcohol Abuse and Alcoholism
037 Drug Literature Index
LA English
SL English
AB Objective: The aim of this study was to test the hypothesis that, because of abnormalities in serotonergic neurotransmission that may underlie craving and impulsive behavior, **fluoxetine** treatment differentially affects drinking among type B alcoholics, who are characterized by high levels of both premorbid vulnerability and alcohol-related problems. Methods: Using a k-means clustering procedure, alcohol-dependent subjects from a placebo- controlled trial of **flu xetine** were grouped into low-risk/severity

(type A: n = 60) and high-risk/severity (type B: n = 35) groups. Multivariate analysis of covariance (with pretreatment measures as covariates) evaluated the affects of Alcoholic Subtype, Medication Group, Treatment Completion, and their interactions on measures of drinking, both during the 12-week treatment period and a 6-month follow-up period. Results: Although there were no main effects of Alcoholic Subtype or Medication Group, subjects who completed the treatment trial showed significantly better drinking-related outcomes. There was also an interaction of Alcoholic Subtype by Medication Group during treatment. Among type B subjects, **fluoxetine** treatment resulted in poorer drinking-related outcomes than placebo treatment. Among type A subjects, there was no affect of Medication Group. This interactive affect did not persist during the 6-month follow-up period. Conclusions: Alcoholic subtypes identified by cluster analysis seem to be differentially responsive to the affects of **fluoxetine** treatment on drinking-related outcomes. Serotonergic abnormalities previously identified among a subgroup of alcoholics who are also characterized by impulsivity and severity of alcohol dependence may help to explain the differential medication effect. Based on these findings, it is recommended that, in the absence of a comorbid mood or anxiety disorder, **fluoxetine** not be used to maintain abstinence or reduce drinking in high- risk/severity alcoholics.

L16 ANSWER 11 OF 12 TOXLIT
AN 1995:73175 TOXLIT
DN CA-122-322641E
TI Fluorimetric determination of **fluoxetine** hydrochloride.
AU Atmaca S
CS Fac. Pharmacy, Univ. Istanbul, Beyazit Istanbul
SO Pharmazie, (1995). Vol. 50, No. 4, pp. 300-1.
CODEN: PHARA. ISSN. 0031-7144.
CY Turkey
DT Journal; Article; (JOURNAL ARTICLE)
FS CA
LA English
OS CA 122:322641
EM 199509
AB **Fluoxetine** (I) has been widely used for the treatment of depression in recent years. This report presents a simple, sensitive and specific fluorimetric method for the detn. of I in capsules by using 7-chloro-4-nitrobenzofurazan (NBD-Cl) as fluorescence labeling reagent. The reaction between I and NBD-Cl proceeded in alk. medium. The results of the pH study indicated that max. fluorescence was obtained at pH 8.5. The derivatization reaction was studied at different temps. and at various periods. The optimum molar ratio of reagent to I was 30. Fluorescence intensity and the position of the emission maxima were dependent on the nature of the solvent used. The deriv. had max. intensity in

EtOAc and it was stable in this solvent for at least 1 wk at 4.degree. in the dark. Relative std. deviations (RSD) were <0.67%, indicating reproducibility. There was no interference from most of the common ingredients such as magnesium trisilicate, di-Me polysiloxane, magnesium stearate, **lactose**, starch and CM-cellulose.

L16 ANSWER 12 OF 12 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.
AN 92178847 EMBASE
TI Evaluation of chronic diarrhea. Article two in the series.
AU Soergel K.H.
CS Department of Medicine, Medical College of Wisconsin, Milwuakee, WI, United States
SO PRACT. GASTROENTEROL., (1992) 16/4 (25-38).
ISSN: 0277-4208 CODEN: PRGAEE
CY United States
DT Journal
FS 003 Endocrinology
004 Microbiology
006 Internal Medicine
008 Neurology and Neurosurgery
017 Public Health, Social Medicine and Epidemiology
030 Pharmacology
048 Gastroenterology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English

=> fil caplu

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FILE LAST UPDATED: 15 Dec 1998 (981215/ED)

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Query 2

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=> d que l22; d que l24

L1            2 SEA FILE=REGISTRY ABB=ON  PLU=ON  (56296-78-7 OR
                54910-89-3)/RN
L17           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  54910-89-3/RN
L18        1313 SEA FILE=CAPLUS ABB=ON  PLU=ON  L17
L19           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  56296-78-7/RN
L20         123 SEA FILE=CAPLUS ABB=ON  PLU=ON  L19
L21        2212 SEA FILE=CAPLUS ABB=ON  PLU=ON  L20 OR L18 OR L1 OR
                FLUOXETINE OR PROZAC
L22          32 SEA FILE=CAPLUS ABB=ON  PLU=ON  L21(S)PHARMACEUT?


L1            2 SEA FILE=REGISTRY ABB=ON  PLU=ON  (56296-78-7 OR
                54910-89-3)/RN
L17           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  54910-89-3/RN
L18        1313 SEA FILE=CAPLUS ABB=ON  PLU=ON  L17
L19           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  56296-78-7/RN
L20         123 SEA FILE=CAPLUS ABB=ON  PLU=ON  L19
L21        2212 SEA FILE=CAPLUS ABB=ON  PLU=ON  L20 OR L18 OR L1 OR
                FLUOXETINE OR PROZAC
L24           1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L21 AND (HY!DROSCOP? OR
                HY!DRO SCOP? OR ANHYDROUS)
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misspelling; see L43

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=> s (l22 or l24) not l8

L25          31 (L22 OR L24) NOT L8

=> d 1-31 .bevstr

L25  ANSWER 1 OF 31  CAPLUS  COPYRIGHT 1998 ACS
AN   1998:712919  CAPLUS
DN   129:280990
TI   Solid, oral pharmaceutical composition of
     fluoxetine with improved organoleptic properties
IN   Yrureragoyena, Belen
PA   Lilly, S.A., Spain
SO   Span., 5 pp.
     CODEN: SPXXAD
DT   Patent
LA   Spanish
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   ES 2103682         A1   19970916      ES 95-1825       19950920
     ES 2103682         B1   19980401
```

AB This invention involves the development of a solid, oral **pharmaceutical fluoxetine** compn. with improved organoleptic properties. The compn. contains 0.4-0.7% fluoxetine hydrochloride, preferably less than 0.5% of sweetener-coloring agent like sodium saccharin or aspartame or neohesperidin or a combination of these. Solvents used: sorbitol, mannitol or a mixt. of these. The compn. can be taken by diabetes patients.

IT **54910-89-3, Fluoxetine 56296-78-7,** **Fluoxetine** hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solid, oral **pharmaceutical** compn. of **fluoxetine** with improved organoleptic properties)

L25 ANSWER 2 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1998:672496 CAPLUS
DN 129:281026
TI Pharmaceutical compositions containing propanamine derivatives and cyclodextrin
IN Geczy, Joseph
PA Therabel Industries S.A., Fr.; Cyclolab Ciklodextrin Kutato-Fejleszto KFT.
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9842382	A1	19981001	WO 98-HU28	19980323

W: AL, AU, BA, BG, BR, CA, CN, CU, CZ, EE, GE, ID, IL, IS, JP, KP, KR, LR, LT, LV, MK, MN, MX, NO, NZ, PL, RO, SI, SK, TR, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI HU 97-632 19970324

AB A pharmaceutical compn., process for its prepn. and method of antidepressive treatment with the compn. contg. a propanamine together with a cyclodextrin in the form of an inclusion complex. The compn. may optionally further contain auxiliary and addnl. excipients materials for oral, parenteral, transdermal, rectal or other medical use. Cyclodextrins of preference are .gamma.-cyclodextrin, a methylated .alpha.-, .beta.- or .gamma.-cyclodextrin, a hydroxypropylated .alpha.-, .beta.- or .gamma.-cyclodextrin, an ionic watersol. .alpha.-, .beta.-, or .gamma.-cyclodextrin polymer, a maltosylated .alpha.-, .beta.- or .gamma.-cyclodextrin. The most preferred inclusion complex contains (.+-.)-, (-)- or (+)-.gamma.-[4-(trifluoromethyl)phenoxy]benzeneprop anamine and .gamma.-cyclodextrin. Thus, sachets were prepd. contg. fluoxetine-.gamma.-cyclodextrin complex 93, citric acid 50, NaHCO3

85, saccharose 120, orange flavor 30, and Mg stearate 465 mg.

IT **54910-89-3DP, Fluoxetine**, cyclodextrin complexes
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(**pharmaceutical** compns. contg. propanamine derivs. and cyclodextrin)

L25 ANSWER 3 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1998:204419 CAPLUS
DN 128:261968
TI Pharmaceutical composition containing combination of atypical antipsychotic and serotonin reuptake inhibitor for treatment of psychoses
IN Bymaster, Franklin Porter; Perry, Kenneth Wayne; Tollefson, Gary Dennis
PA Eli Lilly and Co., USA
SO Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 830864	A1	19980325	EP 97-307375	19970922
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	WO 9811897	A1	19980326	WO 97-US15874	19970909
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9744112	A1	19980414	AU 97-44112	19970909
PRAI	US 96-26884		19960923		
	WO 97-US15874		19970909		

AB Pharmaceutical compns. contg. combination of atypical antipsychotics and serotonin reuptake inhibitors are useful for the treatment of psychoses. Form II olanzapine (I) polymorph was prepd. by heating I at 76.degree. for 30 min in Et acetate and crystn. Hard gelatin capsules contained I 25, fluoxetin hydrochloride 20, starch 150, and magnesium stearate 10 mg.

IT **54910-89-3, Fluoxetine 56296-78-7, Fluoxetine** hydrochloride
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**pharmac utical** compn. contg. combination of atypical antipsychotic and serotonin reuptake inhibitor for treatment of psychoses)

L25 ANSWER 4 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1998:66098 CAPLUS
DN 128:145351
TI Novel transdermal formulations for the administration of fluoxetine
IN Gale, Robert M.; Nelson, Melinda K.; Cormier, Michel J. N.; Gupta, Suneel K.; Campbell, Patricia S.
PA Alza Corporation, USA
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9802169	A2	19980122	WO 97-US12335	19970715
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9736018	A1	19980209	AU 97-36018	19970715
PRAI	US 96-12727		19960715		
	WO 97-US12335		19970715		

AB Compn. of matter for application to a body surface or membrane to administer fluoxetine by permeation through the body surface or membrane, the compn. comprising fluoxetine to be administered, at a therapeutically effective rate, alone or in combination with a permeation enhancer or mixt. A preferred embodiment is directed to the transdermal administration of fluoxetine at reduced skin irritation levels wherein fluoxetine, preferably provided as fluoxetine acetate, is coadministered with a corticosteroid such as hydrocortisone. Also disclosed are drug delivery devices contg. the fluoxetine or fluoxetine and enhancer compn. and methods for the transdermal administration of the fluoxetine and fluoxetine/enhancer compn. The flux of a 10% fluoxetine in 90% oil/petrolatum through human cadaver skin was 20.mu.g/cm2. The addn. of 10% glycerol monolaurate to the formulation increased the flux by by 5 fold.

L25 ANSWER 5 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1997:803807 CAPLUS
DN 128:48490
TI Preparation of amino acid derivatives as pharmaceuticals for

treatment of neurological and neuropsychiatric disorders
IN Ognyanov, Vassil Iliya; Borden, Laurence; Bell, Stanley Charles; Zhang, Jing
PA Trophix Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9745115	A1	19971204	WO 97-US9450	19970529
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9731530	A1	19980105	AU 97-31530	19970529

PRAI US 96-655912 19960531
US 96-656063 19960531
US 97-807682 19970227
US 97-808754 19970227
WO 97-US9450 19970529
OS MARPAT 128:48490
AB Amino acid derivs. R2RxRyXR1NR3(R3*)nCR4R4*R5 [X = N, C (R2 not present when X = N); R2 = H, alkyl, alkoxy, cyano, alkanoyl, etc.; Rx, Ry = aryl, heteroaryl, adamantyl, or nonarom. ring linked to X via a single bond, alkylene, etc.; R1 = alkylene, iminooxyethylene, etc.; R3 = H, alkyl, (un)substituted Ph or phenylalkyl, etc.; R3* = alkyl, O; n = 0, 1; R4, R4* = H, alkyl, hydroxyalkyl; R5 = (un)substituted carbamoyl, carboxy, aminosulfonyl, phosphoryl, etc.] were prepd. as pharmaceuticals for treatment of neurol. and neuropsychiatric disorders. Thus, N-(4,4-diphenyl-3-butenyl)glycine Et ester was by alkylation of glycine Et ester hydrochloride with 4-bromo-1,1-diphenyl-1-butene. Binding assays to measure interaction of compds. with the glycine site on the NMDA receptor are illustrated.
IT **54910-89-3, Fluoxetine**
RL: RCT (Reactant)
(prepn. of amino acid derivs. as **pharmaceuticals** for treatment of neurol. and neuropsychiatric disorders)

L25 ANSWER 6 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1997:749843 CAPLUS
DN 127:336743
TI Batch and flow injection fluorimetric determination of fluoxetine

AU Martin, M. I. Gonzalez; Perez, C. Gonzalez
CS Departamento de Quimica Analitica, Nutricion y Bromatologia. Facultad de Quimica Universidad de Salamanca, Salamanca, 37008, Spain
SO Anal. Lett. (1997), 30(14), 2493-2502
CODEN: ANALBP; ISSN: 0003-2719
PB Marcel Dekker, Inc.
DT Journal
LA English
AB A method for the fluorimetric detn. of fluoxetine in continuous and discontinuous systems is reported. The method is based on the hydrolysis of fluoxetine in acid medium. The fluorescent product has a spectrum with excitation and emission maxima at 253 and 306 nm, resp. The method was applied to the detn. of **fluoxetine** in **pharmaceutical** products.

L25 ANSWER 7 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1997:367536 CAPLUS
DN 127:60207
TI Carcinogenicity testing and the evaluation of regulatory requirements for pharmaceuticals
AU Contrera, Joseph F.; Jacobs, Abigail C.; DeGeorge, Joseph J.
CS Office Testing and Research and Office of Review Management, U.S. Food and Drug Admin., Center for Drug Evaluation and Research, Rockville, MD, 20857, USA
SO Regul. Toxicol. Pharmacol. (1997), 25(2), 130-145
CODEN: RTOPDW; ISSN: 0273-2300
PB Academic
DT Journal
LA English
AB Database The results of rat and mouse carcinogenicity studies for 282 human pharmaceuticals in the FDA database were analyzed and compared as part of an International Conference on Harmonization (ICH) evaluation of rodent carcinogenicity studies and their utility for carcinogenicity testing. A majority of the carcinogenicity studies in the FDA database were carried out in Sprague-Dawley-derived rats and Swiss-Webster-derived CD-1 mice in contrast to Fisher 344 rats and B6C3F1 mice employed in National Toxicol. Program (NTP) studies. Despite the differences in rodent strains, the relative proportion of compds. with pos. findings (44.3%) and the degree of overall concordance between rats and mice (74.1%) in the FDA database were similar to the NTP rodent carcinogenicity database. Carcinogenicity studies in two rodent species are necessary primarily to identify trans-species tumorigens, which are considered to pose a relatively greater potential risk to humans than single species pos. compds. Two-year carcinogenicity studies in both rats and mice may not be the only means of identifying transpecies tumorigens. Sufficient experience is now available for some alternative in vivo carcinogenicity models to support their

application as complementary studies in combination with a single 2-yr carcinogenicity study to identify trans-species tumorigens. Our anal. of the rodent carcinogenicity studies supports such an approach for assessing carcinogenic potential without compromising the public health.

IT **54910-89-3, Fluoxetine**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(rat and mouse carcinogenicity studies and evaluation of regulatory requirements for **pharmaceuticals**)

L25 ANSWER 8 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1997:90421 CAPLUS
DN 126:99331
TI Use of tachykinin antagonists in combination with serotonin agonists or serotonin reuptake inhibitors for the manufacture of a medicament for the treatment of common cold or allergic rhinitis
IN Johnson, Kirk Willis; Phebus, Lee Alan
PA Lilly, Eli, and Co., USA
SO Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 747049	A1	19961211	EP 96-304183	19960606
	R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	WO 9641633	A1	19961227	WO 96-US8336	19960603
	W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN				
	RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9659661	A1	19970109	AU 96-59661	19960603
PRAI	US 95-74		19950608		
	WO 96-US8336		19960603		

AB Methods are provided for the treatment or amelioration of the symptoms of the common cold or allergic rhinitis which comprise administering to a mammal in need thereof a combination of a tachykinin receptor antagonist and either a serotonin agonist or a selective serotonin reuptake inhibitor. The administration may be concurrent or sequential, with either of the two activities being administered first. Compd. prepn. and active-ingredient formulations are included.

IT **54910-89-3, Fluoxetine**
RL: BAC (Biological activity or effector, except adverse); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)
(tachykinin antagonist combination with serotonin agonist or serotonin reuptake inhibitor for treatment of common cold or allergic rhinitis, compd. prepn., and **pharmaceutical** formulations)

L25 ANSWER 9 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1996:747349 CAPLUS
DN 126:94894
TI An alternative method for the determination of chloride in pharmaceutical drug substances using HPLC and evaporative light-scattering detection
AU Risley, Donald S.; Peterson, Jeffrey A.; Griffiths, Kristi L.; McCarthy, Sharon
CS Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA
SO LC-GC (1996), 14(12), 1040-1042, 1046-1047
CODEN: LCGCE7; ISSN: 0888-9090
PB Advanstar
DT Journal
LA English
AB Researchers traditionally have analyzed inorg. ions such as chloride in pharmaceutical drug substances by ion chromatog. (IC) with cond. detection or titrn. methods. The authors have developed a new quant. method for the detn. of chloride in pharmaceutical drug substances using high performance liq. chromatog. (HPLC) with evaporative light-scattering detection. They compare the analyses of chloride in 17 pharmaceutical drug substances (hydrochloride salts) using HPLC anal. with evaporative light-scattering detection (ELSD) against the theor. chloride content based on empirical formulas. In addn., they statistically compare chloride results obtained by IC, capillary electrophoresis, and titrn. methods with results obtained by HPLC-ELSD.
IT **54910-89-3, Fluoxetine**
RL: AMX (Analytical matrix); ANST (Analytical study)
(detn. of chloride in **pharmaceuticals** by HPLC using light-scattering detection)

L25 ANSWER 10 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1996:699467 CAPLUS
DN 125:339201
TI Estimation of **fluoxetine** hydrochloride in **pharmaceutical** dosage forms by HPLC.
AU Bawde, Nagesh; Sharma, Naresh; Hatiari, S. T.; Sehgal, Rahul
CS Nestor Pharmaceuticals Limited, Faridabad, 121 001, India
SO East. Pharm. (1996), 39(463), 127-129
CODEN: EAPHA6; ISSN: 0012-8872
DT Journal
LA English
AB An expedient and specific H.P.L.C. method for the detn. of

Fluoxetine Hydrochloride in **pharmaceutical** dosage forms have been developed and validated. Diln. of the std. and the sample solns. were made in mobile phase suitably and filtered through 0.45 nm filter. The sample and the test solns. were run on a C18 column packed with 5 .mu. particle size using Acetonitrile 550 mL. and 450 mL buffer soln. of 0.5% orthophosphoric acid in water ((pH) adjusted to 6.5 with triethylamine) as mobile phase and the flow rate was kept at 1 mL/min. The eluted peak was quantified by measuring the absorbance at 229 nm using a variable wave length U.V. detector. It obeys Beer's Law in the concn. range of 100-700 ug/mL. For further validation of this method, a recovery study was conducted, adding known quantity of the drug to the test soln. and calcd. the percentage recovery in each case.

IT **59333-67-4, Fluoxetine** hydrochloride
RL: ANT (Analyte); ANST (Analytical study)
(estn. of **fluoxetine** hydrochloride in **pharmaceutical** dosage forms by HPLC)

L25 ANSWER 11 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1996:675005 CAPLUS
DN 126:9584
TI Modeling and simulation of SMB technology for pharmaceutical and fine chemical applications
AU Dandekar, Hemant W.; Chandhok, Ajay K.; Priegnitz, James W.
CS UOP, Des Plaines, IL, 60017, USA
SO Fundam. Adsorpt., Proc. Int. Conf., 5th (1996), Meeting Date 1995, 243-250. Editor(s): LeVan, M. Douglas. Publisher: Kluwer, Boston, Mass.
CODEN: 63PBA5
DT Conference
LA English
AB The application of UOP Sorbex simulated moving bed (SMB) technol. for pharmaceutical sepns. is described. The marked differences between pharmaceutical and conventional bulk sepns., makes predicting initial starting conditions difficult unless a well-defined modeling strategy is used. The dispersion and mass transfer coeffs. of the adsorbent bed are detd. using well-known correlations. Langmuir isotherms were measured using breakthrough tests. A 1-D, axial-dispersed plug flow, linear driving-force model for the SMB process is solved using finite differences and a Newton Raphson iterative procedure. The model results are compared with exptl. results for sepn. of 3-chloro-1-phenyl-propanol (CPP), a drug intermediate in the manuf. of fluoxetine.

IT **54910-89-3P, Fluoxetine**
RL: IMF (Industrial manufacture); PUR (Purification or recovery); PREP (Preparation)
(simulated moving bed sepn. technol. for **pharmaceuticals** and fine chems.)

L25 ANSWER 12 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1996:364484 CAPLUS
DN 125:19200
TI Electrochemical reduction of fluoxetine
AU Brett, A. M. Oliveira; Lima, Jose L. F. C.; Roque da Silva, A. M. Spinola
CS Fc. Ciencias e Tecnol., Univ. de Coimbra, Coimbra, 3000, Port.
SO Port. Electrochim. Acta (1995), 13(Dec.), 509-512
CODEN: PEACEZ
DT Journal
LA English
AB The electrochem. redn. of fluoxetine was studied using a hanging mercury drop electrode in different buffer solns. up to pH 13 and with concns. of fluoxetine varying from 1.0.times.10-6M to 5.0.times.10-5M. A very strong adsorption of fluoxetine on the electrode was obsd. and the shape of the cyclic voltammograms suggests that in these conditions it corresponds to a quasi-reversible system for absorbed species. The results obtained for the electrochem. quantification of fluoxetine in five pharmacol. formulations existing in the Portuguese market were compared.

L25 ANSWER 13 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1996:357034 CAPLUS
DN 125:19027
TI Oral pharmaceutical and/or nutritional microcapsules comprising polymer coating
IN Autant, Pierre; Selles, Jean-Philippe; Soula, Gerard
PA Flamel Technologies, Societe Anonyme, Fr.
SO Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 709087	A1	19960501	EP 95-420286	19951018
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	FR 2725623	A1	19960419	FR 94-12759	19941018
	FR 2725623	B1	19970221		
	CA 2160762	AA	19960419	CA 95-2160762	19951017
	ZA 9508762	A	19960509	ZA 95-8762	19951017
	WO 9611675	A2	19960425	WO 95-FR1369	19951018
	WO 9611675	A3	19960620		
	W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE,				

IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9538077	A1	19960506	AU 95-38077	19951018
BR 9509286	A	19971014	BR 95-9286	19951018
JP 10509427	T2	19980914	JP 95-513006	19951018

PRAI FR 94-12759 19941018
WO 95-FR1369 19951018

AB Microcapsules contg. pharmaceutical or nutritional agents having particle size .ltoreq.1000.mu.m and are coated with film-forming polymers are disclosed. Aciclovir 2800.6, PVP 87.1, and water 1301 g were mixed and granulated, then 300 g of microparticles thus obtained were coated with a soln. contg. Et cellulose 120.30, PVP 13.00, castor oil 13.00, magnesium stearate 16.26, acetone 1284.70, and isopropanol 142.70 g.

IT **54910-89-3, Fluoxetine**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral **pharmaceutical** and/or nutritional microcapsules comprising polymer coating)

L25 ANSWER 14 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1996:190940 CAPLUS
DN 124:220513
TI Use of pharmaceutical agents interacting with 5-HT receptors for alleviation or treatment of the immune dysfunction related to infection with human immunodeficiency viruses (HIV) or related viruses
IN Hofmann, Bo Arne
PA Den.
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9601106	A1	19960118	WO 95-DK285	19950705

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9528804	A1	19960125	AU 95-28804	19950705

PRAI DK 94-810 19940706
WO 95-DK285 19950705

AB Pharmaceutical agents which interact with 5-HT receptors are used for alleviation or treatment of the immune dysfunction related to infection with human immunodeficiency viruses (HIV) or related

viruses, e.g. as seen in pre-AIDS and AIDS. The interaction may be via an immune cell receptor, e.g. present on T cells, the receptor being structurally or functionally related to the 5-HT receptors or subtypes thereof present on cells in the nervous system. Preferred agents are sumatriptan, buspirone, gepirone, ipsapirone, 5-hydroxytryptamine, and 8-hydroxy-2-(di-N-propylamino)tetralin (DPAT), or derivs. or precursors of these agents.

IT **54910-89-3, Fluoxetine 54910-89-3D, Fluoxetine**, derivs. and precursors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**pharmaceutical** agents interacting with 5-HT receptors for treatment of immune dysfunction related to infection with HIV or related virus)

L25 ANSWER 15 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1996:65002 CAPLUS
DN 124:127144
TI Oral pharmaceutical controlled-release liquid suspension containing oils and polymers and antioxidants
IN Modi, Pankaj
PA Can.
SO Can. Pat. Appl., 18 pp.
CODEN: CPXXEB
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2143070	AA	19950823	CA 95-2143070	19950221

PRAI US 94-199933 19940222

AB A controlled-release oral formulation for use with a variety of drugs, e.g. anti-Parkinsonian, cardiovascular and anti-epileptic drugs are formed in liq. suspension form. The ingredients in the suspension are water, and edible oil and a stabilizer for the liq. suspension, at least one pharmaceutically active ingredient, at least two water sol. biodegradable polymers, and optionally with at least one antioxidant to prevent degrdn. and oxidn. of the pharmaceutically active ingredients. A typical tsp dose of anti-Parkinson liq. suspension contains 15-150 mg carbidopa, 50-1500 mg levodopa, 100-300 mg of a combination of polyvinyl alc. and polysucrose, 10-50 mg oil, 5-15 mg antioxidant, e.g. vitamin E, 5-20 mg stabilizer, 10-15 mg colorants, 10-15 mg natural flavoring agents and 5 mL water.

IT **54910-89-3, Fluoxetine**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral **pharmaceutical** controlled-release liq. suspensions contg. oils and polymers and antioxidants)

L25 ANSWER 16 OF 31 CAPLUS COPYRIGHT 1998 ACS

AN 1995:990929 CAPLUS
DN 124:15528
TI Methods and compositions for treating depression and other disorders using optically pure S(+) fluoxetine
IN Young, James W.; Barberich, Timothy J.
PA Sepracor Inc., USA
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9528152	A1	19951026	WO 95-US4508	19950410
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5589511	A	19961231	US 94-228240	19940415
	AU 9522874	A1	19951110	AU 95-22874	19950410

PRAI US 94-228240 19940415
US 90-566655 19900813
US 91-793036 19911115
US 93-67380 19930526
WO 95-US4508 19950410

AB Methods and compns. are disclosed utilizing the pure S(+) isomer of fluoxetine which is a potent antidepressant and appetite suppressant substantially free of unwanted, adverse toxic or psychol. effects. In addn., methods and compns. are disclosed utilizing the pure S(+) isomer of fluoxetine which is useful in treating migraine headaches, pain, in particular chronic pain, obsessive-compulsive disorders, sexual dysfunction and memory disorders. Further, methods and compns. for treating a condition alleviated or improved by inhibition of serotonin uptake in serotonergic neurons and platelets in a human using optically pure S(+) fluoxetine are disclosed.

L25 ANSWER 17 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1995:716960 CAPLUS
DN 123:93291
TI Microparticular pharmaceutical compositions in micellar form
IN Cho, Young W.
PA Isotech Medical, Inc., USA
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9512385	A1	19950511	WO 94-US12351	19941103
	W: CA, JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2175494	AA	19950511	CA 94-2175494	19941103
	EP 726761	A1	19960821	EP 95-901066	19941103
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
PRAI	US 93-146747	19931103			
	WO 94-US12351	19941103			

AB A pharmaceutical compn. comprises microparticles in micelles. The microparticles contain at least one of each a pharmaceutically-active agent, a water or lipid-sol. or -miscible phospholipid, a nonionic surfactant having an HLB value of .gtoreq. 15 and .ltoreq. 6, and a water-sol. or -miscible sterol compd. The compn. is prepd. by admixing the components, micronizing the admixt. to form microparticles, and suspending the microparticles in at least one fatty acid of chain length of C14 or less to form microparticles in micelles. The invention may be useful in the oral administration of drugs and other therapeutic agents, as well as for the trans-umbilico-dermal administration of such drugs and therapeutic agents. Oral insulin formulations with enhanced bioavailability and activity were prepd.

IT **54910-89-3, Fluoxetine**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microparticular **pharmaceutical** compns. in micellar form)

L25 ANSWER 18 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1994:708162 CAPLUS
DN 121:308162
TI The stability of extemporaneously prepared solutions of fluoxetine hydrochloride
AU Marshall, Thomas M.; Mullen, Michael V.
CS Eli Lilly and Co., Indianapolis, IN, USA
SO Pharm. Sci. Commun. (1994), 4(3), 143-5
CODEN: PSCME3; ISSN: 1351-6337
DT Journal
LA English
AB This study reports on the chem., phys. and microbiol. stability of liq. fluoxetine-HCl at concns. less than the com. available product. Results of the study, conducted using various com. and extemporaneously prepd. vehicles, show that fluoxetine-HCl is chem. stable for at least 60 days when stored at temps. up to 30.degree.. The microbiol. properties of the preservative are not compromised by diln. nor are there changes in the phys. characteristics of the

soln.

L25 ANSWER 19 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1994:491554 CAPLUS
DN 121:91554
TI Stability of **fluoxetine** hydrochloride in **fluoxetine** solution diluted with common **pharmaceutical** diluents
AU Peterson, Jeffrey A.; Risley, Donald S.; Anderson, Philip N.; Hostettler, Kurt F.
CS Pharm. Sci. Div., Eli Lilly and Co., Indianapolis, IN, USA
SO Am. J. Hosp. Pharm. (1994), 51(10), 1342-5
CODEN: AJHPA9; ISSN: 0002-9289
DT Journal
LA English
AB **Fluoxetine** hydrochloride was stable for eight weeks in **fluoxetine** soln. dild. to 1 or 2 mg/mL with common **pharmaceutical** diluents and stored at 5 or 30 .degree.C.
IT **59333-67-4**, **Fluoxetine** hydrochloride
RL: PRP (Properties)
(stability of, in **pharmaceutical** diluent solns.)

L25 ANSWER 20 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1994:116847 CAPLUS
DN 120:116847
TI Biodegradable controlled release melt-spun delivery system
IN Fuisz, Richard C.
PA Fuisz Technologies, Ltd., USA
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9324154	A1	19931209	WO 93-US5307	19930602
	W: AU, CA, HU, JP, KR, PL, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5518730	A	19960521	US 92-893238	19920603
	AU 9344058	A1	19931230	AU 93-44058	19930602
	AU 665844	B2	19960118		
	JP 07507548	T2	19950824	JP 93-500877	19930602
	EP 746342	A1	19961211	EP 93-914373	19930602
	R: BE, CH, DE, DK, FR, GB, IE, IT, LI, LU, NL, SE				
PRAI	US 92-893238	19920603			
	WO 93-US5307	19930602			

AB Biodegradable controlled-release delivery systems using melt-spun biodegradable polymers as carriers for bio-effecting agents such as

pharmaceutical actives are disclosed. Oral dose forms as well as implants are described. For example, polyglycolide was melt-spun in combination with various drugs such as vancomycin, gentamicin, tolmetin, diphenhydramine, ibuprofen, and insulin and controlled drug release was demonstrated.

IT **59333-67-4**, **Fluoxetine** hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled-release **pharmaceuticals** formed by flash-flow melt-spinning contg., biodegradable polymers as carriers in)

L25 ANSWER 21 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1993:656550 CAPLUS
DN 119:256550
TI Alkyl-substituted cellulose-based sustained-release oral drug dosage forms
IN Shell, John W.
PA Depomed Systems, Inc., USA
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9318755	A1	19930930	WO 93-US2420	19930317
	W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, RU				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
	AU 9338114	A1	19931021	AU 93-38114	19930317
	AU 668386	B2	19960502		
	EP 632720	A1	19950111	EP 93-907548	19930317
	EP 632720	B1	19981111		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 07507059	T2	19950803	JP 93-516691	19930317
	AT 173159	E	19981115	AT 93-907548	19930317
PRAI	US 92-858320	19920325			
	US 92-986952	19921208			
	WO 93-US2420	19930317			

AB Sustained-release oral dosage forms, e.g. tablets, contg. alkyl-substituted cellulose derivs. are disclosed. Once the tablets disintegrates in the stomach to disperse the particle, they absorb water and swell and become slippery, and thus their retention in the stomach is enhanced. The absorbed water from the gastric fluid dissolves the drug entrapped in the particles and the resulting soln. diffuses from the dispersed particles and assuring that no solid drug, which is more irritating, contacts the mucosal tissue.

Hydroxypropyl cellulose and aspirin (I) 15 at various proportions were mixed and compressed into 3mm diam. cylindrical pellets. The cumulative release of I was monitored in simulated gastric fluid. The release of I over a period of 7h was steady as compared to the conventional I tablets which released >90% I within 0.5 h.

IT **54910-89-3**
RL: BIOL (Biological study)
(sustained-release oral **pharmaceuticals** contg. alkyl cellulose derivs. and)

L25 ANSWER 22 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1993:603106 CAPLUS
DN 119:203106
TI Preparation of and **pharmaceutical** formulations utilizing pure S(+) enantiomer **fluoxetine**
IN Young, James W.; Barberich, Timothy J.
PA Sepracor, Inc., USA
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9309769	A1	19930527	WO 92-US888	19920205
	W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
	AU 9213736	A1	19930615	AU 92-13736	19920205
	EP 612242	A1	19940831	EP 92-906545	19920205
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
	AU 9718917	A1	19970619	AU 97-18917	19970417
PRAI	US 91-793036		19911115		
	WO 92-US888		19920205		

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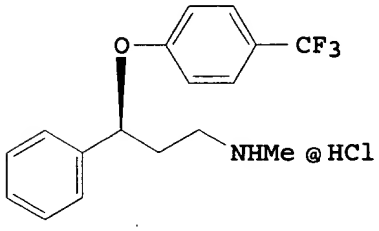

I

AB The title S enantiomer of fluoxetine I has been reported to have

enhanced antidepressant properties without the numerous side effects assocd. with racemic fluoxetine. Fluoxetine hydrochloride S enantiomer I is prepd. from (+)-epoxycinnamyl alc. in 4 steps and is claimed to be useful (no data) in treatment of schizophenia, Huntington's Chorea, memory disorders, obesity, migraine headaches, alcoholism, pain, obsessive-compulsive disorder, etc. Numerous I-contg. pharmaceutical formulations are presented.

L25 ANSWER 23 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1993:175943 CAPLUS
DN 118:175943
TI Gas liquid chromatographic determination of **fluoxetine** hydrochloride in its **pharmaceutical** dosage forms
AU Raghuveer, S.; Avadhanulu, A. B.; Pantulu, A. R. R.
CS Qual. Control Dep., IDPL, Hyderabad, 500 037, India
SO Indian Drugs (1993), 30(2), 83-6
CODEN: INDRBA; ISSN: 0019-462X
DT Journal
LA English
AB A sensitive gas chromatog. method for the detn. of fluoxetine in dosage forms was based on the use of 3% XE-60 and 5% OV-1 columns with flame ionization detection. Isonicotine acid hydrazide and chlorpropamide were the internal stds. N was used as the carrier gas at a flow rate of 20 mL/min.
IT **54910-89-3**, **Fluoxetine**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in **pharmaceuticals** by gas chromatog.)

L25 ANSWER 24 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1992:639836 CAPLUS
DN 117:239836
TI Methods of use and compositions of R(-)-fluoxetine
IN Young, James W.; Barberich, Timothy J.; Teicher, Martin H.
PA USA
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9213452	A1	19920820	WO 92-US833	19920203
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
AU 9214290	A1	19920907	AU 92-14290	19920203
US 5708035	A	19980113	US 95-446348	19950522
US 5648396	A	19970715	US 95-486056	19950607

PRAI US 91-650385 19910204
US 91-793062 19911115
US 91-794264 19911115
WO 92-US833 19920203
US 93-80374 19930618

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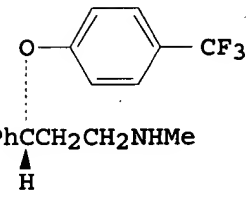

PhCCH2CH2NHMe
H

I

AB R(-)-Fluoxetine (I) is prepd. as an antidepressant and appetite suppressant substantially free of adverse effects. It is also used for treatment of migraine headaches, pain, and obsessive compulsive disorders. I was prepd. from (R)-3-phenyl-1,3-dihydroxypropane by mesylation, reaction with MeNH2, and then with 4-chlorobenzotrifluoride. Tablets and capsules contg. I were prepd.

L25 ANSWER 25 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1992:201263 CAPLUS
DN 116:201263
TI GC estimation of **fluoxetine** and tolnaftate from their **pharmaceutical** preparations
AU Sane, R. T.; Jani, A. B.; Ghadge, J. K.; Vaidya, A. J.; Kotwal, S. S.
CS S. P. Mandali's T. D. M. Lab., Bombay, 400 022, India
SO Indian Drugs (1992), 29(5), 237-9
CODEN: INDRBA; ISSN: 0019-462X
DT Journal
LA English
AB **Fluoxetine** and tolnaftate were detd. in **pharmaceuticals** by gas chromatog. on a glass column packed with 3% OV-225 or OV-210 on Chromosorb W-HP with a flame-ionization detector and chlorpheniramine maleate as the internal std. The recovery for fluoxetine and tolnaftate was 101.2 and 98.7-100.9%, resp. The relative std. deviation was 1.81-2.16%.
IT **54910-89-3, Fluoxetine**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in **pharmaceuticals** by gas chromatog.)

L25 ANSWER 26 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1992:136283 CAPLUS
DN 116:136283

TI Pharmaceutical preparations for treatment of depression and/or migraine
IN Johnson, Edward Stewart
PA Beecham Group PLC, UK
SO PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9200103	A1	19920109	WO 91-GB992	19910620
	W: AU, CA, JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	AU 9180726	A1	19920123	AU 91-80726	19910620
	ZA 9104920	A	19920429	ZA 91-4920	19910626
PRAI	GB 90-14354		19900628		
	GB 90-14364		19900628		
	GB 90-14365		19900628		
	GB 90-14367		19900628		
	WO 91-GB992		19910620		

AB A pharmaceutical compn. comprises 2-3 active ingredients selected from a 5-HT3 receptor antagonist, a 5-HT reuptake inhibitor, and a 5-HT1 receptor agonist, as a combined prepn. for simultaneous, sep., or sequential use in therapy.
IT **54910-89-3D, Fluoxetine**, mixt. with 5-HT receptor agonist and 5HT3 receptor antagonists
RL: BIOL (Biological study)
(**pharmaceutical** compn. contg., for treatment of depression or migraine)

L25 ANSWER 27 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1990:590895 CAPLUS
DN 113:190895
TI Preparation and formulation of **fluoxetine** analog as serotonin antagonist
IN Fuller, Ray Ward; Robertson, David Wayne; Wong, David Taiwai
PA Lilly, Eli, and Co., USA
SO Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 369685	A2	19900523	EP 89-311634	19891110
	EP 369685	A3	19910327		
	EP 369685	B1	19950419		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				

	CA 2002483	AA	19900514	CA 89-2002483	19891108
	ZA 8908513	A	19910731	ZA 89-8513	19891108
	DK 8905602	A	19900515	DK 89-5602	19891109
	AU 8944516	A1	19900517	AU 89-44516	19891109
	AU 622942	B2	19920430		
	HU 58041	A2	19920128	HU 89-5848	19891109
	SU 1750417	A3	19920723	SU 89-4742384	19891109
	CN 1042704	A	19900606	CN 89-108468	19891110
	JP 02193951	A2	19900731	JP 89-293785	19891110
	JP 2776919	B2	19980716		
	ES 2071663	T3	19950701	ES 89-311634	19891110
	US 5250571	A	19931005	US 92-873520	19920421

PRAI US 88-270177 19881114
US 89-412687 19890926
US 90-486478 19900228
US 90-615201 19901119

OS MARPAT 113:190895

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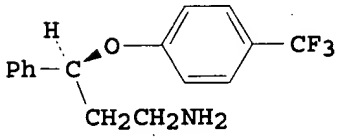


I

AB (S)-Norfluoxetine (I), an effective serotonin antagonist useful in treating depression, is prepd. A soln. of 4.046 (S)-1-phthalimido-1-phenyl-1-propanol and **anhyd.** N2H4 in EtOH was refluxed under N to give 210 mg (S)-3-amino-1-phenyl-1-propanol, which (1.74 g) was heated with a slurry of 60% NaH in oil and AcNMe2 at 70.cxa. and then 1.54 mL 4-FC6H4CF3 at 100.degree. to give 1.5 g I. I showed inhibition of 3H-serotonin uptake in vitro at IC50 of 69 nM, vs. 1051 nM with (R)-norfluoxetine and 127 nM with (R)-**fluoxetine**. Capsule, tablet, and suppository formulations were given.

IT **54910-89-3DP**, **Fluoxetine**, analogs
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of as serotonin antagonist)

L25 ANSWER 28 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1990:510802 CAPLUS
DN 113:110802
TI Method using fluoxetine for the treatment of nicotine withdrawal syndrome
IN Hapworth, William E.; Hapworth, Mada S.
PA USA
SO U.S., 9 pp.

CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

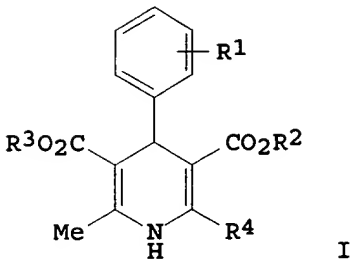
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 4940585	A	19900710	US 89-312954	19890217

AB The title treatment comprises administration of a compn. contg. a **pharmaceutically** acceptable carrier and **fluoxetine**, so as to inhibit serotonin reuptake in the neurohormonal pathways of the central nervous system and provide physiol. relief from the withdrawal symptoms. The dose of fluoxetine is approx. 5-40 mg/day. Other therapeutic agents, e.g. major or minor tranquilizers or other antidepressants, may be administered in conjunction with the fluoxetine. Thus, a patient with a 42 pack-year history entered an educational/behavioral modification program and accomplished a stop date for smoking. Post cessation of smoking, he experienced moderate withdrawal symptoms, complaining of irritability, some depression, extreme sugar cravings, and a sense of phys. bloating. The patient was begun 5 days after cessation on 20 mg fluoxetine/day and experienced within 3 h a sense of alleviation of all of the above symptoms. Nine other case studies are included.

L25 ANSWER 29 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1989:625327 CAPLUS
DN 111:225327
TI Dihydropyridine calcium antagonists as antidepressants, and synergistic antidepressant pharmaceutical mixtures containing them
IN Traber, Jorg; Horstmann, Harald
PA Troponwerke G.m.b.H und Co. K.-G., Fed. Rep. Ger.
SO Eur. Pat. Appl., 7 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 293714	A1	19881207	EP 88-108234	19880524
EP 293714	B1	19910605		
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, SE				
DE 3718398	A1	19881222	DE 87-3718398	19870602
AT 64094	E	19910615	AT 88-108234	19880524
ES 2045008	T3	19940116	ES 88-108234	19880524
JP 63310867	A2	19881219	JP 88-132887	19880601
JP 2701042	B2	19980121		
US 4956361	A	19900911	US 89-370425	19890623
PRAI DE 87-3718398		19870602		
US 88-197066		19880519		
EP 88-108234		19880524		

OS MARPAT 111:225327
GI



I

AB Dihydropyridines with Ca antagonist properties (I: R1 = NO2, halo, CF3, OCHF2, :NON: that is condensed to the Ph ring; R2, R3 = alkyl that is optionally substituted by alkoxy, OH, halo, N-methyl-N-benzylamino; R4 = cyano, alkyl that is optionally substituted by OH, halo) are used in pharmaceuticals with antidepressant efficacy. Mice were placed into a cyclindrical vessel filled with water; after their attempts to escape failed, the animals fell into depression-induced immobilization. Animals were treated with antidepressants i.p. and with I orally 30 min prior to the expt. Mice treated with 10 mg/kg imipramine remained depressed for 174.6 s; animals treated with 20 mg/kg nifedipine for 101.3 s, and animals treated with 20 mg/kg nifedipine and 10 mg/kg imipramine remained depressed for 24.2 s. Ca antagonists, such as verapamil (phenylalkylamine) or diltiazem (benzothiazepine), lacked an antidepressant effect in comparison to nifedipine or nitrendipine.

IT **54910-89-3D, Fluoxetine**, mixts. with dihydropyridine calcium antagonists
RL: BIOL (Biological study)
(synergistic antidepressant **pharmaceutical** contg.)

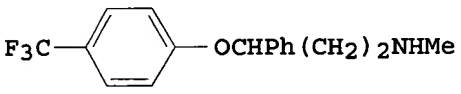
L25 ANSWER 30 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1987:149481 CAPLUS
DN 106:149481
TI Method for improving memory using fluoxetine
IN Cherkin, Arthur; Flood, James F.; Wong, David T.
PA Lilly, Eli, and Co. , USA
SO U.S., 5 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	US 4647591	A	19870303	US 85-785411	19851007

AB A method for treating amnesia and for improving memory retention in mammals comprises administering **fluoxetine** (I) or a **pharmaceutically** acceptable salt of I. I (15 mg/kg) injected into mice after training, counteracted anisomycin- or scopolamine-induced amnesia.

L25 ANSWER 31 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1978:609084 CAPLUS
DN 89:209084
TI The effect of fluoxetine on warfarin metabolism in the rat and man
AU Rowe, Howard; Carmichael, Ralph; Lemberger, Louis
CS Lilly Lab. Clin. Res., Wishard Mem. Hosp., Indianapolis, Indiana, USA
SO Life Sci. (1978), 23(8), 807-11
CODEN: LIFSAK; ISSN: 0024-3205
DT Journal
LA English
GI



I

AB Fluoxetine (I) [54910-89-3], a selective blocker of serotonin uptake, inhibited the metab. of warfarin [81-81-2] in rats. In contrast, after a single dose or 7 daily doses of I to human subjects, no inhibition of warfarin metab. was obsd. The possible effects of I on drug metab. are discussed.

=> fil uspat; d que l29; d que l31

FILE 'USPATFULL' ENTERED AT 13:54:56 ON 15 DEC 1998
CA INDEXING COPYRIGHT (C) 1998 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 8 Dec 1998 (19981208/PD)
FILE LAST UPDATED: 9 Dec 1998 (19981209/ED)
HIGHEST PATENT NUMBER: US5848438
CA INDEXING IS CURRENT THROUGH 9 Dec 1998 (19981209/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 8 Dec 1998 (19981208/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: May 1998
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 1998

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Searcher : Shears 308-4994

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>>> USPTO Manual of Classifications in the /NCL, /INCL, and /RPCL <<<
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>>> USPTO/MOC subject headings and subheadings. Thesauri are also <<<
>>> available for the WIPO International Patent Classification <<<
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This file contains CAS Registry Numbers for easy and accurate substance identification.

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                 OR HY!DRO SCOP? OR ANHYDROUS)
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↑ misspelling see L46

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                 54910-89-3)/RN
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L18         1313 SEA FILE=CAPLUS ABB=ON  PLU=ON  L17
L19            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  56296-78-7/RN
L20          123 SEA FILE=CAPLUS ABB=ON  PLU=ON  L19
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                 FLUOXETINE OR PROZAC
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                 HY!DRO SCOP? OR ANHYDROUS)

=> s (l29 or l31) not l14

L32           16 (L29 OR L31) NOT L14

=> d 1-16 bib abs

L32  ANSWER 1 OF 16  USPATFULL
                        Searcher  :  Shears  308-4994
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AN 1998:154512 USPATFULL
TI Process for preparing N-methyl-3-(P-trifluoromethylphenoxy)-3-phenyl-propylamine and salts thereof in a highly pure form
IN Arosio, Roberto, Civate, Italy
Beratto, Stefano Giovanni Vittorio, Milan, Italy
Rossetti, Vittorio, Milan, Italy
PA Laporte Organics Francis S.p.A., Milan, Italy (non-U.S. corporation)
PI US 5847214 981208
AI US 97-889162 970707 (8)
PRAI IT 96-MI1438 960711
DT Utility
EXNAM Primary Examiner: Raymond, Richard L.
LREP Modiano, Guido; Josif, Albert
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 447
AB The present invention relates to a process for preparing N-methyl-3-(p-trifluoromethylphenoxy)-3-phenyl-propylamine and pharmaceutically acceptable acid addition salts thereof. The process in accordance with the present invention comprises reacting 1-phenyl-3-(N-methylamine) propane-1-ol with 1-chloro-4-trifluoromethylbenzene, in the presence of an hydroxide of an alkaline metal in a dipolar aprotic solvent non saponifiable in reaction conditions. The process in accordance with the present invention further comprises a final crystallization step which allows to obtain the active ingredient in a highly pure crystalline form.

L32 ANSWER 2 OF 16 USPATFULL
AN 1998:95533 USPATFULL
TI Bisindoles as tachykinin receptor antagonists
IN Hipskind, Philip A., New Palestine, IN, United States
Lobb, Karen L., Indianapolis, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)
PI US 5792760 980811
AI US 97-838960 970423 (8)
DT Utility
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Kessinger, Ann M.
LREP Gaylo, Paul J.; Boone, David E.
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2220
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a series of substituted bisindole propanamides which are useful as tachykinin receptor antagonists and as serotonin agonists. This invention also provides methods for the treatment of related disorders as well as pharmaceutical formulations which employ these novel compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L32 ANSWER 3 OF 16 USPATFULL
AN 1998:92024 USPATFULL
TI Compounds having effects on serotonin-related systems
IN Audia, James E., Indianapolis, IN, United States
Hibschman, David J., Bargersville, IN, United States
Krushinski, Jr., Joseph H., Indianapolis, IN, United States
Mabry, Thomas E., Indianapolis, IN, United States
Nissen, Jeffrey S., Fishers, IN, United States
Rasmussen, Kurt, Fishers, IN, United States
Rocco, Vincent P., Indianapolis, IN, United States
Schaus, John M., Zionsville, IN, United States
Thompson, Dennis C., Indianapolis, IN, United States
Wong, David T., Indianapolis, IN, United States
PA Eli Lilly Company, Indianapolis, IN, United States (U.S. corporation)
PI US 5789402 980804
AI US 95-471121 950606 (8)
RLI Continuation-in-part of Ser. No. US 95-373823, filed on 17 Jan 1995, now abandoned
DT Utility
EXNAM Primary Examiner: Berch, Mark L.; Assistant Examiner: Kifle, Bruck
LREP Palmberg, Arleen; Boone, David E.
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5961
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A series of hetero-oxy alkanamines are effective pharmaceuticals for the treatment of conditions related to or affected by the reuptake of serotonin and by the serotonin 1.sub.A receptor. The compounds are particularly useful for alleviating the symptoms of nicotine and tobacco withdrawal, and for the treatment of depression and other conditions for which serotonin reuptake inhibitors are used.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L32 ANSWER 4 OF 16 USPATFULL
AN 1998:69187 USPATFULL
TI Asymmetric synthesis catalyzed by transition metal complexes with new chiral ligands

IN Zhang, Xumu, State College, PA, United States
PA The Penn State Research Foundation, University Park, PA, United States (U.S. corporation)
PI US 5767276 980616
AI US 96-729469 961011 (8)
DT Utility
EXNAM Primary Examiner: Lambkin, Deborah
LREP Monahan, Thomas J.
CLMN Number of Claims: 35
ECL Exemplary Claim: 1
DRWN 11 Drawing Figure(s); 10 Drawing Page(s)
LN.CNT 2032
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A chiral ligand having the following structure: ##STR1## wherein AR is any aromatic and/or ring structure, and R is selected from the group consisting of aryl, oxygenated aryl, alkyl, oxygenated alkyl, AR, oxygenated AR and combinations thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L32 ANSWER 5 OF 16 USPATFULL
AN 1998:61855 USPATFULL
TI Preparation and use of 2-methyl-5-phenylisoxazolidine
IN Theriot, Kevin J., Baton Rouge, LA, United States
PA Albemarle Corporation, Richmond, VA, United States (U.S. corporation)
PI US 5760243 980602
AI US 97-901235 970725 (8)
DT Utility
EXNAM Primary Examiner: McKane, Joseph
LREP Pippenger, Philip M.
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 499
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB (a) An alkali metal base (hydroxide, oxide, carbonate, bicarbonate or sesquicarbonate), an acid addition salt of N-methylhydroxylamine, and (iii) water are mixed together to form a reaction mixture in which the acid of the acid addition salt has been neutralized. (b) Reaction mixture from (a) and formaldehyde or formalin are mixed together and the resultant mixture is subjected to reaction conditions that produce a reaction mixture in which N-methylnitrone has been formed. (c) Reaction mixture from (b) and styrene are mixed and the resultant mixture to subjected to reaction conditions that produce a reaction mixture in which 2-methyl-5-phenylisoxazolidine has been formed. Preferably, 2-methyl-5-phenylisoxazolidine formed in (c) is hydrogenated such that N-methyl-3-phenyl-3-hydroxypropylamine is

formed, which in turn is reacted with 4-halobenzotrifluoride such that N-methyl-3-phenyl-3-[4-trifluoromethyl)phenoxy]propylamine is formed. Conversion of the N-methyl-3-phenyl-3-[4-trifluoromethyl)phenoxy]propylamine to its racemic hydrochloride salt provides fluoxetine hydrochloride, a widely used antidepressant.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L32 ANSWER 6 OF 16 USPATFULL
AN 1998:42357 USPATFULL
TI Compounds having effects on serotonin-related systems
IN Hibschman, David J., Bargersville, IN, United States
Krushinski, Jr., Joseph H., Indianapolis, IN, United States
Rasmussen, Kurt, Fishers, IN, United States
Rocco, Vincent P., Indianapolis, IN, United States
Schaus, John M., Zionsville, IN, United States
Thompson, Dennis C., Indianapolis, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)
PI US 5741789 980421
AI US 95-467434 950606 (8)
RLI Continuation-in-part of Ser. No. US 95-373823, filed on 17 Jan 1995, now abandoned
DT Utility
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Kifle, Bruck
LREP Palmberg, Arleen; Boone, David E.
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5902
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A series of hetero-oxy alkanamines are effective pharmaceuticals for the treatment of conditions related to or affected by the reuptake of serotonin and by the serotonin 1.sub.A receptor. The compounds are particularly useful for alleviating the symptoms of nicotine and tobacco withdrawal, and for the treatment of depression and other conditions for which serotonin reuptake inhibitors are used.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L32 ANSWER 7 OF 16 USPATFULL
AN 1998:4633 USPATFULL
TI Methods of use and compositions of R(-) fluoxetine
IN Young, James W., Palo Alto, CA, United States
Barberich, Timothy J., Concord, MA, United States
Teicher, Martin H., Wellesley, MA, United States

PA Sepracor Inc., Marlborough, MA, United States (U.S. corporation)
McLean Hospital, Belmont, MA, United States (U.S. corporation)
PI US 5708035 980113
AI US 95-446348 950522 (8)
RLI Continuation of Ser. No. US 93-80374, filed on 18 Jun 1993, now abandoned which is a continuation-in-part of Ser. No. US 91-650385, filed on 4 Feb 1991, now abandoned which is a continuation-in-part of Ser. No. US 91-793062, filed on 15 Nov 1991, now abandoned which is a continuation-in-part of Ser. No. US 91-794264, filed on 15 Nov 1991, now abandoned
DT Utility
EXNAM Primary Examiner: Criares, Theodore J.
LREP Pennie & Edmonds LLP
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 946
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method and composition are disclosed utilizing the pure R(-) isomer of fluoxetine which is a potent antidepressant and appetite suppressant substantially free of adverse effects. In addition, a method and composition are disclosed utilizing the pure R(-) isomer of fluoxetine which is useful to treat migraine headaches, pain, in particular chronic pain, psychoactive substance abuse disorders and obsessive compulsive disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L32 ANSWER 8 OF 16 USPATFULL
AN 97:61727 USPATFULL
TI Methods for treating depression and other disorders using optically pure R (-) fluoxetine and monoamine oxidase inhibitor
IN Young, James W., Palo Alto, CA, United States
Barberich, Timothy J., Concord, MA, United States
Teicher, Martin H., Wellesley, MA, United States
PA Sepracor Inc., Marlbrough, MA, United States (U.S. corporation)
PI US 5648396 970715
AI US 95-486056 950607 (8)
RLI Continuation of Ser. No. US 93-80374, filed on 18 Jun 1993, now abandoned which is a continuation-in-part of Ser. No. US 91-650385, filed on 4 Feb 1991, now abandoned Ser. No. Ser. No. US 91-793062, filed on 15 Nov 1991, now abandoned And Ser. No. US 91-794264, filed on 15 Nov 1991, now abandoned
DT Utility
EXNAM Primary Examiner: Criares, Theodore J.
LREP Pennie & Edmonds
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 932
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method and composition are utilizing the pure R(-) isomer of fluoxetine which is a potent antidepressant and appetite suppressant substantially free of adverse effects. In addition, a method and composition are disclosed utilizing the pure R(-) isomer of fluoxetine which is useful to treat migraine headaches, pain, in particular chronic pain, psychoactive substance abuse disorders and obsessive compulsive disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L32 ANSWER 9 OF 16 USPATFULL
AN 97:38539 USPATFULL
TI Compounds having effects on serotonin-related systems
IN Audia, James E., Indianapolis, IN, United States
Hibschman, David J., Bargersville, IN, United States
Krushinski, Jr., Joseph H., Indianapolis, IN, United States
Mabry, Thomas E., Indianapolis, IN, United States
Nissen, Jeffrey S., Fishers, IN, United States
Rasmussen, Kurt, Fishers, IN, United States
Rocco, Vincent P., Indianapolis, IN, United States
Schaus, John M., Zionsville, IN, United States
Thompson, Dennis C., Indianapolis, IN, United States
Wong, David T., Indianapolis, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)
PI US 5627196 970506
AI US 95-468948 950606 (8)
RLI Continuation-in-part of Ser. No. US 95-373823, filed on 17 Jan 1995, now abandoned
DT Utility
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Bottino, Anthony
LREP Jones, Joseph A.; Boone, David E.
CLMN Number of Claims: 56
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5947
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A series of hetero-oxy alkanamines are effective pharmaceuticals for the treatment of conditions related to or affected by the reuptake of serotonin and by the serotonin 1.sub.A receptor. The compounds are particularly useful for alleviating the symptoms of nicotine and tobacco withdrawal, and for the treatment of depression and other conditions for which serotonin reuptake inhibitors are used.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L32 ANSWER 10 OF 16 USPATFULL
AN 97:25037 USPATFULL
TI Compounds having effects on serotonin-related systems
IN Audia, James E., Indianapolis, IN, United States
Krushinski, Jr., Joseph H., Indianapolis, IN, United States
Rasmussen, Kurt, Fishers, IN, United States
Rocco, Vincent P., Indianapolis, IN, United States
Schaus, John M., Zionsville, IN, United States
Thompson, Dennis C., Indianapolis, IN, United States
Wong, David T., Indianapolis, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)
PI US 5614523 970325
AI US 95-470512 950606 (8)
RLI Continuation-in-part of Ser. No. US 95-373823, filed on 17 Jan 1995, now abandoned
DT Utility
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Bottino, Anthony
LREP Jones, Joseph A.; Boone, David E.
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5755
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A series of hetero-oxy alkanamines are effective pharmaceuticals for the treatment of conditions related to or affected by the reuptake of serotonin and by the serotonin 1.sub.A receptor. The compounds are particularly useful for alleviating the symptoms of nicotine and tobacco withdrawal, and for the treatment of depression and other conditions for which serotonin reuptake inhibitors are used.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L32 ANSWER 11 OF 16 USPATFULL
AN 97:17918 USPATFULL
TI Compositions and methods for enhanced drug delivery
IN Hale, Ron L., Woodside, CA, United States
Lu, Amy, Los Altos, CA, United States
Solas, Dennis, San Francisco, CA, United States
Selick, Harold E., Belmont, CA, United States
Oldenburg, Kevin R., Fremont, CA, United States
Zaffaroni, Alejandro C., Atherton, CA, United States
PA Affymax Technologies N.V., Middlesex, England (non-U.S. corporation)
PI US 5607691 970304
AI US 95-449188 950524 (8)

RLI Continuation of Ser. No. US 93-164293, filed on 9 Dec 1993, now abandoned which is a continuation-in-part of Ser. No. US 93-77296, filed on 14 Jun 1993, now abandoned which is a continuation-in-part of Ser. No. US 92-898219, filed on 12 Jun 1992, now abandoned And a continuation-in-part of Ser. No. US 93-9463, filed on 27 Jan 1993, now abandoned
DT Utility
EXNAM Primary Examiner: Levy, Neil S.
LREP Stevens, Lauren L.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5349
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to methods of delivering pharmaceutical agents across membranes, including the skin layer or mucosal membranes of a patient. A pharmaceutical agent is covalently bonded to a chemical modifier, via a physiologically cleavable bond, such that the membrane transport and delivery of the agent is enhanced.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L32 ANSWER 12 OF 16 USPATFULL
AN 97:7930 USPATFULL
TI Compositions containing sertraline and a 5-HT.sub.1D receptor agonist or antagonist
IN Howard, Harry R., New York, NY, United States
Macor, John E., New York, NY, United States
Chenard, Bertrand L., New York, NY, United States
Sprouse, Jeffrey S., New York, NY, United States
Schulz, David W., New York, NY, United States
PA Pfizer Inc., New York, NY, United States (U.S. corporation)
PI US 5597826 970128
AI US 94-306230 940914 (8)
DT Utility
EXNAM Primary Examiner: Acquah, Samuel A.
LREP Richardson, Peter C.; Ginsburg, Paul H.; Butterfield, Garth
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3659
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel compositions containing the serotonin selective re-uptake inhibitor (SSRI), preferably (1S-cis)-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-N-methyl-1-naphthalenamine, and an agonist or antagonist of the serotonin 1 (5-HT.sub.1) receptor and to the use of such compositions for treating or preventing a condition selected from mood disorders,

including depression, seasonal affective disorders and dysthmia, anxiety disorders including generalized anxiety disorder and panic disorder; agoraphobia, avoidant personality disorder; social phobia; obsessive compulsive disorder; post-traumatic stress disorder; memory disorders including dementia, amnestic disorders and age-associated memory impairment; disorders of eating behavior, including anorexia nervosa and bulimia nervosa; obesity; cluster headache; migraine; pain; Alzheimer's disease; chronic paroxysmal hemicrania; headache associated with vascular disorders; Parkinson's disease, including dementia in Parkinson's disease, neuroleptic-induced parkinsonism and tardive dyskinesias; endocrine disorders such as hyperprolactinaemia; vasospasm (particularly in the cerebral vasculature); hypertension; disorders in the gastrointestinal tract where changes in motility and secretion are involved; sexual dysfunction, including premature ejaculation; and chemical dependencies.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L32 ANSWER 13 OF 16 USPATFULL
AN 96:106493 USPATFULL
TI Compounds having effects on serotonin-related systems
IN Krushinski, Jr., Joseph H., Indianapolis, IN, United States
Rasmussen, Kurt, Fishers, IN, United States
Rocco, Vincent P., Indianapolis, IN, United States
Schaus, John M., Zionsville, IN, United States
Thompson, Dennis C., Indianapolis, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)
PI US 5576321 961119
AI US 95-468900 950606 (8)
RLI Continuation-in-part of Ser. No. US 95-373823, filed on 17 Jan 1995, now abandoned
DT Utility
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Bottino, Anthony
LREP Jones, Joseph A.; Boone, David E.
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5725
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A series of hetero-oxy alkanamines are effective pharmaceuticals for the treatment of conditions related to or affected by the reuptake of serotonin and by the serotonin 1.sub.A receptor. The compounds are particularly useful for alleviating the symptoms of nicotine and tobacco withdrawal, and for the treatment of depression and other conditions for which serotonin reuptake inhibitors are used.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L32 ANSWER 14 OF 16 USPATFULL
AN 93:54899 USPATFULL
TI Production of fluoxetine and new intermediates
IN Schwartz, Eduard, Rehovot, Israel
Kaspi, Joseph, Givataim, Israel
Itov, Zinovi, Rishon-Lezion, Israel
Pilarski, Gidon, Holon, Israel
PA Teva Pharmaceutical Industries Ltd., Jerusalem, Israel (non-U.S. corporation)
PI US 5225585 930706
AI US 92-931312 920818 (7)
PRAI IL 91-99316 910827
DT Utility
EXNAM Primary Examiner: Raymond, Richard L.
LREP Oliff & Berridge
CLMN Number of Claims: 12
ECL Exemplary Claim: 1,10
DRWN No Drawings
LN.CNT 385
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB 4-methyl-3-[(4-trifluormethyl)phenoxy]-3-phenyl propylamine (I) is prepared by reacting 3-dimethylamino-1-phenyl-1-propanol (III) with haloformate (VIII) to obtain a substituted propyl carbamate (IX) which is hydrolyzed under basic conditions to yield methylamino-1-phenyl-1-propanol (X). The methylamino-1-phenyl-1-propanol is then converted to fluoxetine (I) by reaction with 4-halobenzotrifluoride (XI).

In the process certain substituted carbamates are obtained as intermediates.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L32 ANSWER 15 OF 16 USPATFULL
AN 92:29716 USPATFULL
TI Methods and compositions for treating depression using optically pure fluoxetine
IN Young, James W., Still River, MA, United States
Barberich, Timothy J., Concord, MA, United States
PA Sepracor, Inc., Marlborough, MA, United States (U.S. corporation)
PI US 5104899 920414
AI US 90-566655 900813 (7)
DT Utility
EXNAM Primary Examiner: Friedman, S. J.
LREP Pennie & Edmonds
CLMN Number of Claims: 13

ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 518
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method and composition are disclosed utilizing the pure S(+) isomer of fluoxetine, which is a potent antidepressant substantially free of adverse toxic or psychological effects, having a rapid onset of action and a high response rate.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L32 ANSWER 16 OF 16 USPATFULL
AN 91:96535 USPATFULL
TI Process for producing optically pure 2-phenoxyphenylalkylamines
IN Brown, Herbert C., West Lafayette, IN, United States
PA Aldrich Chemical Company, Inc., Milwaukee, WI, United States (U.S. corporation)
PI US 5068432 911126
AI US 91-649160 910201 (7)
RLI Continuation of Ser. No. US 89-364831, filed on 12 Jun 1989, now abandoned which is a division of Ser. No. US 88-175178, filed on 30 Mar 1988, now patented, Pat. No. US 4868344, issued on 19 Sep 1989
DT Utility
EXNAM Primary Examiner: Cintins, Marianne; Assistant Examiner: Nguyen, Jessica H.
LREP Niblack, Joyce R.; Niblack, Robert L.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 554
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A process for producing the optically pure (+)- or (-) isomer of a phenyl- or substituted- phenylalkanolamine compounds having pharmacologic activity without the need for resolution processes and novel intermediates useful in the process including optically pure haloalcohols are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his l38

(FILE 'BIOSIS, MEDLINE, EMBASE, LIFESCI, BIOTECHDS, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, PROMT, TOXLIT, TOXLINE, DRUGU, DRUGNL, DRUGB' ENTERED AT 13:55:44 ON 15 DEC 1998)
L38 6 S L35 AND (HYDROSCOP? OR HYDRO SCOP? OR ANHYDROUS)

=> d que

Searcher : Shears 308-4994

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L1             2 SEA FILE=REGISTRY ABB=ON  PLU=ON  (56296-78-7 OR
                 54910-89-3)/RN
L17            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  54910-89-3/RN
L18         1313 SEA FILE=CAPLUS ABB=ON  PLU=ON  L17
L19            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  56296-78-7/RN
L20          123 SEA FILE=CAPLUS ABB=ON  PLU=ON  L19
L21         2212 SEA FILE=CAPLUS ABB=ON  PLU=ON  L20 OR L18 OR L1 OR
                 FLUOXETINE OR PROZAC
L35        30900 SEA L21
L39            0 SEA L35 AND NONHY!ROSCOP?

=> d que l38

L1             2 SEA FILE=REGISTRY ABB=ON  PLU=ON  (56296-78-7 OR
                 54910-89-3)/RN
L17            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  54910-89-3/RN
L18         1313 SEA FILE=CAPLUS ABB=ON  PLU=ON  L17
L19            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  56296-78-7/RN
L20          123 SEA FILE=CAPLUS ABB=ON  PLU=ON  L19
L21         2212 SEA FILE=CAPLUS ABB=ON  PLU=ON  L20 OR L18 OR L1 OR
                 FLUOXETINE OR PROZAC
L35        30900 SEA L21
L38            6 SEA L35 AND (HY!ROSCOP? OR HY!RO SCOP? OR ANHYDROUS)

=> s l38 not l15

L40            5 L38 NOT L15

=> dup rem l40

PROCESSING COMPLETED FOR L40
L41            5 DUP REM L40 (0 DUPLICATES REMOVED)

=> d 1-5 bib abs; fil caplu

L41  ANSWER 1 OF 5  SCISEARCH  COPYRIGHT 1998 ISI (R)
AN   97:463839  SCISEARCH
GA   The Genuine Article (R) Number: XE323
TI   Radiosynthesis and PET imaging of [N-methyl-C-11]LY257327 as a
     tracer for 5-HT transporters
AU   ZeaPonce Y (Reprint); Baldwin R M; Stratton M D; AlTikriti M; Soufer
     R; Schaus J M; Innis R B
CS   NEW YORK STATE PSYCHIAT INST & HOSP, DEPT NEUROSCI, 722 W 168TH ST,
     BOX 28, NEW YORK, NY 10032 (Reprint); YALE UNIV, SCH MED, DEPT
     PSYCHIAT, W HAVEN, CT 06516; YALE UNIV, SCH MED, DEPT DIAGNOST
     RADIOL, W HAVEN, CT 06516; YALE VA POSITRON EMISS TOMOG CTR, VET
     AFFAIRS MED CTR, W HAVEN, CT; ELI LILLY & CO, LILLY CORP CTR, LILLY
     RES LABS, INDIANAPOLIS, IN 46285
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CYA USA
SO NUCLEAR MEDICINE AND BIOLOGY, (APR 1997) Vol. 24, No. 3, pp. 251-254.
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD, ENGLAND OX5 1GB.
ISSN: 0883-2897.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 19
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB No-carrier-added [N-methyl-C-11]LY257327 was synthesized by methylation of the free base of the desmethyl precursor LY214281 with [C-11]methyl iodide in **anhydrous** acetonitrile. Synthesis time was 52 +/- 3 min, radiochemical yield (based on [C-11]methyl iodide) was 35 +/- 8%, radiochemical purity was 99 +/- 1%, and specific activity at EOB was 3900 +/- 1300 mCi/mu mol. Two in vivo studies in baboon were carried out before and after pretreatment with the selective serotonin reuptake inhibitor citalopram. The first experiment showed high accumulation of radioactivity in midbrain, striatum, and thalamus, with slightly lower accumulation in the occipital and cerebellum regions. The radioactivity concentration peaked 5 min postinjection, decreasing steadily for the rest of the scanning time. The second experiment (blocked with citalopram) showed only partial inhibition of incorporation in all of the same brain regions, Although [N-methyl-C-11]LY257327 displayed high brain uptake (5% of injected dose at 5 min postinjection) and localized in serotonergic areas of the brain, its target-to-nontarget ratio and its insensitivity to citalopram blocking suggest that its accumulation is dominated by nonspecific uptake. Therefore, [N-methyl-C-11]LY257327 is not a useful agent for measuring serotonin reuptake sites in vivo by positron emission tomography. (C) 1997 Elsevier Science Inc.

L41 ANSWER 2 OF 5 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 97-16737 DRUGU M P G
TI Polymorphism of drugs. An economic challenge?
AU Henck J O; Griesser U J; Burger A
CS Univ.Innsbruck
LO Innsbruck, Austria
SO Pharm.Ind. (59, No. 2, 165-69, 1997) 2 Fig. 1 Tab. 26 Ref.
CODEN: PHINAN ISSN: 0031-711X
AV Univsersitat Innsbruck, Institut fur Pharmakognosie, Josef-Moeller Haus, Innrain 52, A-6020 Innsbruck, Austria. (A.B.).
LA German
DT Journal
FA AB; LA; CT
FS Literature
AN 97-16737 DRUGU M P G
Searcher : Shears 308-4994

AB The polymorphism of drugs is reviewed with reference to pseudopolymorphism (solvation and hydration) and factors influencing the generation of polymorphic drug forms during the manufacturing process. Methods of studying polymorphism and the physical and chemical differences between polymorphic drug forms are dealt with. The solid-state properties of drugs are becoming of increasing economic importance in the pharmaceutical industry.

ABEX Polymorphic or pseudopolymorphic forms have been reported for ranitidine-HCl, nifedipine, enalapril-maleate, fluoxetin-HCl, captopril and diclofenac-sodium (**anhydrous** and tetrahydrated forms), but not for omeprazole, simvastatin, aciclovir, ciprofloxacin, amoxicillin, ciclosporin, lovastatin or amlodipine. The different polymorphic forms can have different properties with respect to stability during storage, release and absorption after dosage, pharmacokinetics and metabolism. Factors affecting the development of polymorphism during drug manufacture include temperature, humidity and the method of tabletting. This makes monitoring during the manufacturing process important in evaluating drug properties. The different forms of ranitidine-HCl have given rise to disputes about the extent of coverage of the patent for this drug. (S67/DAC) Polymorphie von Arzneistoffen. Eine wirtschaftliche Herausforderung?

L41 ANSWER 3 OF 5 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.

AN 94193537 EMBASE

TI Derivatization with acetic anhydride: Applications to the analysis of biogenic amines and psychiatric drugs by gas chromatography and mass spectrometry.

AU Baker G.B.; Coutts R.T.; Holt A.

CS Neurochemical Research Unit, Department of Psychiatry, University of Alberta, Edmonton, Alta. T6G 2R7, Canada

SO J. PHARMACOL. TOXICOL. METHODS, (1994) 31/3 (141-148).
ISSN: 1056-8719 CODEN: JPTMEZ

CY United States

DT Journal

FS 029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index

LA English

SL English

AB Acetylation with acetic anhydride, under both aqueous and **anhydrous** conditions, has been utilized to derivatize various biogenic amines and psychotropic drugs for subsequent analysis by gas chromatography (GC) or gas chromatography-mass spectrometry (GC-MS). Under basic aqueous conditions, acetic anhydride derivatizes phenols and amines but not alcohols; under **anhydrous** conditions, all three functions are acetylated. Primary amines, once derivatized with acetic anhydride, can be further derivatized with other reagents; these diderivatives have

proven useful for subsequent analysis by GC or GC-MS. Examples of applications of derivatization with acetic anhydride to analysis of biogenic amines, antidepressants, antipsychotics, and some of their metabolites are presented.

L41 ANSWER 4 OF 5 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 91-333145 [00] WPIDS
DNC C91-143808
AN 91-333145 [00] WPIDS
AB
ABEQ CA 2037239 A UPAB: 930928
Stable, crystalline (S)-norfluoxetine hydrochloride (I) is new.

Three crystalline forms of (I) have been successfully isolated. They are distinguished by their X-ray powder diffraction patterns.

USE/ADVANTAGE - (I) (in (R) and (S) forms), is a metabolite of **fluoxetine**, used in the treatment of depression. (I) is also a 5-HT blocker, but, as normally prepd., is either amorphous or of poorly defined form, and **hygroscopic**. It is not suitable therefore for use in pharmaceutical prepns. The methods here devised for crystallisation provide stable forms 1 and 3, for use in treating a mammal requiring increased neurotransmission of 5-HT, and form 2, an intermediate for form 1. Forms 1 and 3 are used to treat disorders influenced by 5-HT such as obesity, bulimia, obsessive-compulsive disorders, depression, aggression, alcoholism, pain, pre-menstrual syndrome, loss of memory, anxiety, panic attack, smoking, symptoms of nicotine withdrawal, sleep disorders such as narcolepsy or sleep apnea, urinary incontinence, substance abuse (e.g. cocaine, heroin, amphetamines) dementia, emotional disturbance associated with Alzheimer's disease, and migraine. Following thrombolytic or angioplasty therapy, they aid increase in recanalisation, and prevent restenosis or vasospasm. The forms have little effect on the metabolism of concurrently administered drugs. 0/0

L41 ANSWER 5 OF 5 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 84-37394 DRUGU P
TI Depletions of Central Norepinephrine by Intraventricular Xylamine in Rats.
AU Geyer M A; Gordon J; Adams L M
LO Louisiana, Jolla, California, United States
SO Eur.J.Pharmacol. (100, No. 2, 227-31, 1984) 1 Fig. 1 Tab. 10 Ref.
CODEN: EJPHAZ ISSN: 0014-2999
AV Department of Psychiatry, UCSD T-004, La Jolla, CA 92093, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 84-37394 DRUGU P
AB The effect of producing central norepinephrine (NE) depletions

using intraventricular (i.vt.) injections of xylamine (Xy) was investigated in rats. With ether anesthesia, bilateral injections of Xy reduced hippocampal levels of NE and serotonin (5-HT) without affecting striatal dopamine or 5-HT. Rats treated with a combination of 20 ng/kg i.p. fluoxatine HCl (F; Lilly) and 100 ug Xy showed selective depletion of central NE with no significant changes in 5-HT. Rats treated with Xy alone or in combination with F remained healthy and their overt behaviour remained normal.

ABEX Male Sprague-Dawley rats (250-275 g) were anesthetized with **anhydrous** ether and placed in a stereotaxic apparatus. Some rats received i.p. injections of F prior to surgery. Xy (50 or 100 ug) was administered i.vt.. Brain monoamine levels were assayed by HPLC with electrochemical detection. I.vt. administration of 50 mg Xy reduced hippocampal NE and 5-HT as soon as 48 hr after treatment. Relative to controls, NE was reduced by 34.7% at 24 and by 60% at 48 hr. Hippocampal 5-HT was reduced by 41% and 48.8% at 24 and 48 hr, respectively. 1,15 Or 20 mg/kg of the specific serotonin reuptake blocker, F, given 1 hr before the administration of 50 ug Xy, effectively limited the 5-Ht depletion without affecting the approximately 60% depletion in NE induced by Xy. The depletion in NE produced by 50 ug Xy plus 15 mg/kg F was long-lasting with hypothalamic NE still reduced by 36% 8 days later. Xy-treated animals failed to exhibit post-decapitative convulsions, suggesting depletion of spinal NE. Xy plus F produced a delayed increase in 5 -HT turnover in both hippocampus and striatum.

FILE COVERS 1967 - 15 Dec 1998 VOL 129 ISS 25
FILE LAST UPDATED: 15 Dec 1998 (981215/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

Searcher : Shears 308-4994

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                54910-89-3)/RN
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L19           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  56296-78-7/RN
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=> s l42 not (l8 or l25)

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=> d his l46- ful; s l46 not (l14 or l32)


     (FILE 'USPATFULL' ENTERED AT 14:03:22 ON 15 DEC 1998)
L46           2 SEA ABB=ON  PLU=ON  L21(S)(HY!ROSCOP? OR HY!RO SCOP? OR
                ANHYDROUS OR NONHY!ROSCOP?)
L47           0 L46 NOT (L14 OR L32)

FILE 'MEDLINE' ENTERED AT 14:05:44 ON 15 DEC 1998

 FILE LAST UPDATED: 29 OCT 1998 (19981029/UP).  FILE COVERS 1966 TO DATE.

 MEDLINE UPDATES ON HOLD UNTIL AFTER THE ANNUAL RELOAD HAS BEEN
 COMPLETED.  NOTICE WILL BE GIVEN ONCE THE RELOAD IS COMPLETED AND
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 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
 SUBSTANCE IDENTIFICATION.


L48        2867 SEA FILE=MEDLINE ABB=ON  PLU=ON  FLUOXETINE/CT
L49        5610 SEA FILE=MEDLINE ABB=ON  PLU=ON  LACTOSE/CT
L50           1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L48 AND L49

=> d .beverlymed; fil hom

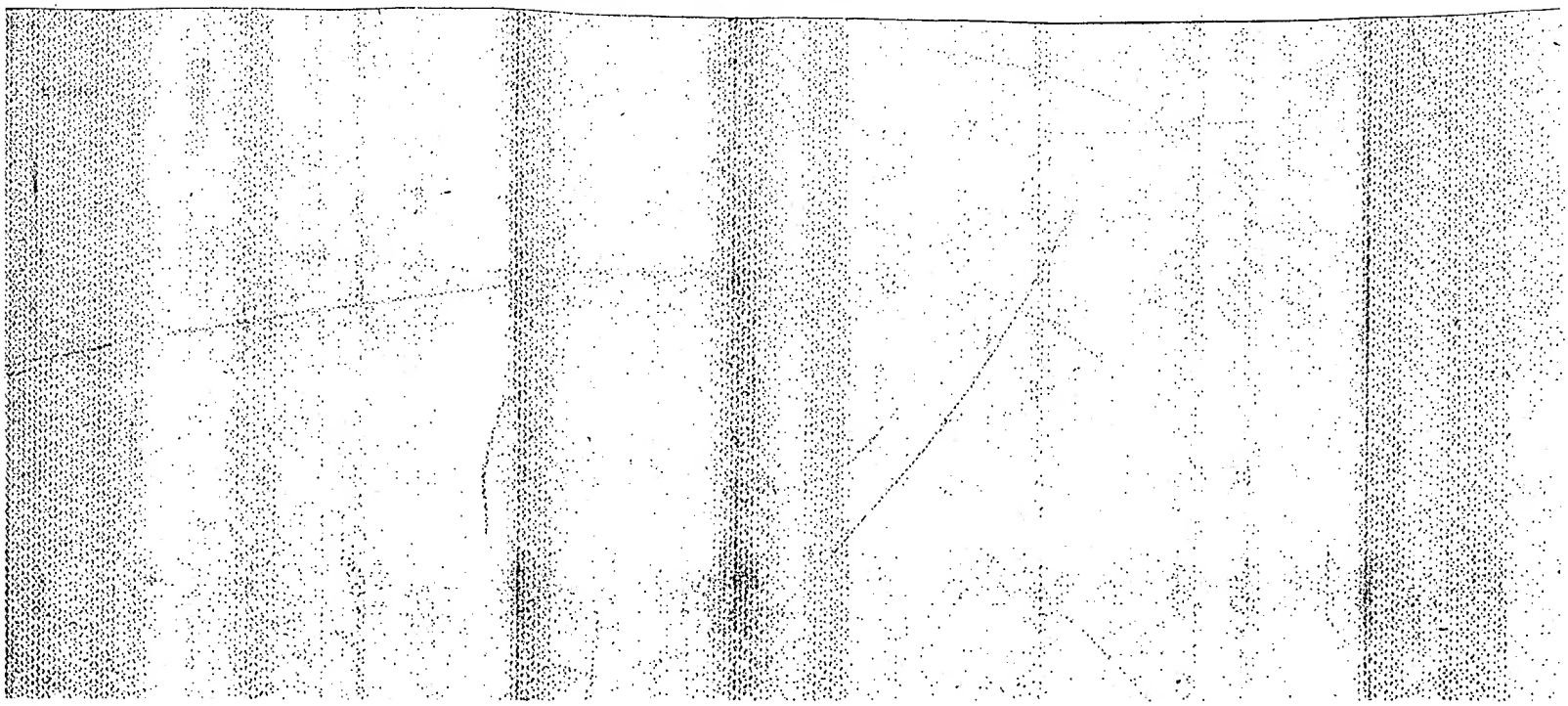

L50  ANSWER 1 OF 1  MEDLINE
AN   1998115055     MEDLINE
TI   Maillard reaction of lactose and fluoxetine hydrochloride, a
     secondary amine.
AU   Wirth D D; Baertschi S W; Johnson R A; Maple S R; Miller M S;
                        Searcher  :  Shears   308-4994
```

Hallenbeck D K; Gregg S M

SO JOURNAL OF PHARMACEUTICAL SCIENCES, (1998 Jan) 87 (1) 31-9.
Journal code: JO7. ISSN: 0022-3549.

AB Analysis of commercially available generic formulations of fluoxetine HCl revealed the presence of lactose as the most common excipient. We show that such formulations are inherently less stable than formulations with starch as the diluent due to the Maillard reaction between the drug, a secondary amine hydrochloride, and lactose. The Amadori rearrangement product was isolated and characterized; the characterization was aided by reduction with sodium borohydride and subsequent characterization of this reduced adduct. The lactose-fluoxetine HCl reaction was examined in aqueous ethanol and in the solid state, in which factors such as water content, lubricant concentration, and temperature were found to influence the degradation. N-Formylfluoxetine was identified as a major product of this Maillard reaction and it is proposed that N-formyl compounds be used as markers for this drug-excipient interaction since they are easy to prepare synthetically. Many characteristic volatile products of the Maillard reaction have been identified by GC/MS, including furaldehyde, maltol, and 2,3-dihydro-3,5-dihydroxy-6-methyl-4 H-pyran-4-one. Close similarity between the degradation products of simple mixtures and formulated generic products was found; however, at least one product decomposed at a rate nearly 10 times that predicted from the simple models. Maillard products have also been identified in unstressed capsules. The main conclusion is that drugs which are secondary amines (not just primary amines as sometimes reported) undergo the Maillard reaction with lactose under pharmaceutically relevant conditions. This finding should be considered during the selection of excipients and stability protocols for drugs which are secondary amines or their salts, just as it currently is for primary amines.

FILE 'HOME' ENTERED AT 14:05:50 ON 15 DEC 1998



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Author(s)

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L51      7648 S REDMOND ?/AU
L52     54689 S BUTLER ?/AU
L53      6608 S WALD ?/AU
L54         0 S L51 AND L52 AND L53
L55         6 S L51 AND (L52 OR L53)
L56        29 S L52 AND L53
L57     68910 S L51 OR L52 OR L53
L58        43 S L57 AND L21
L59        78 S L55 OR L56 OR L58
L60        39 DUP REM L59 (39 DUPLICATES REMOVED)
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L60 ANSWER 1 OF 39 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 1

AN 1998:548533 CAPLUS

DN 129:180143

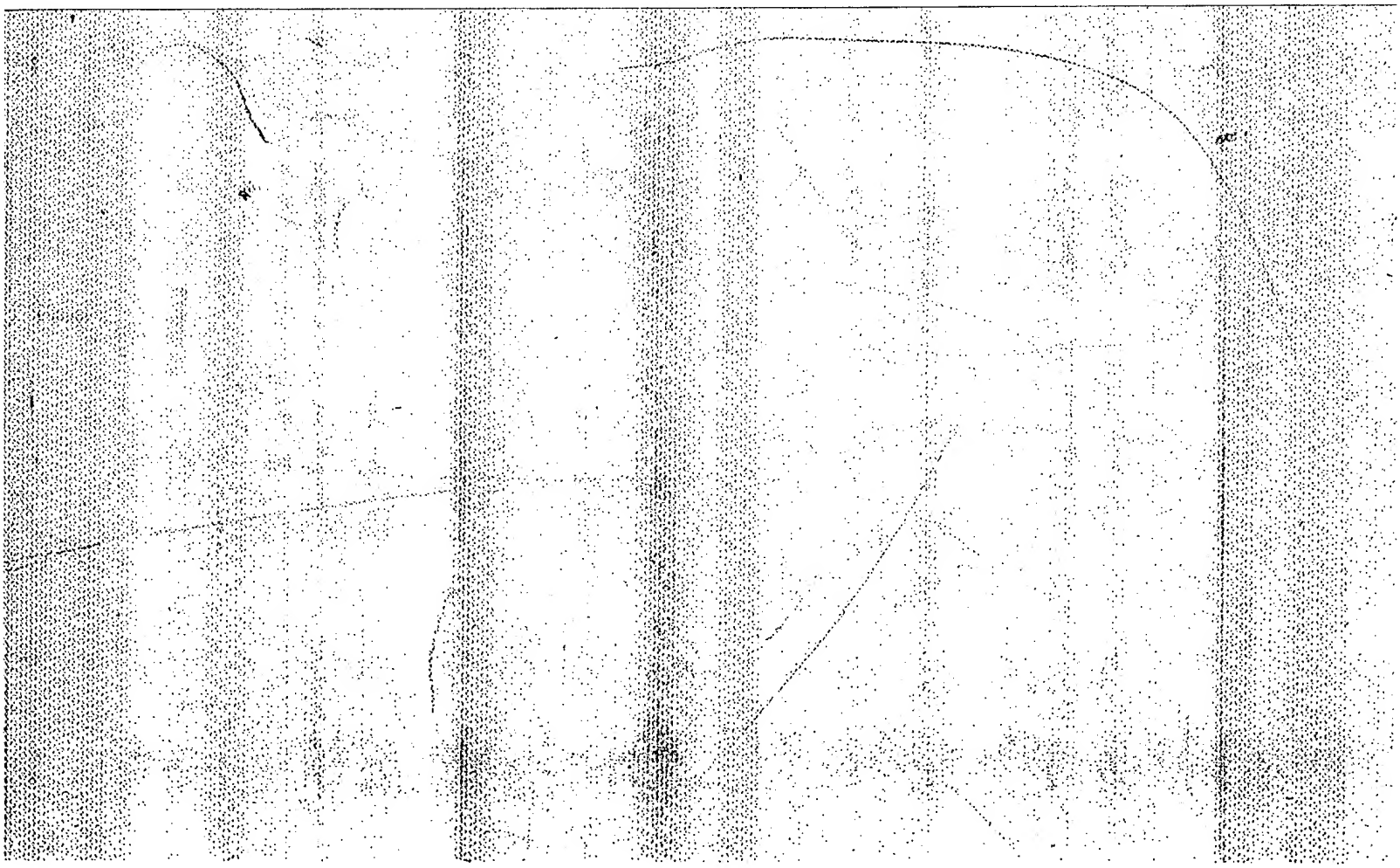
TI Lactose-free, non-hygroscopic and anhydrous pharmaceutical compositions of descarboethoxyloratadine

IN Redmon, Martin P.; **Butler, Hal T.**; **Wald, Stephen A.**; Rubin, Paul D.

PA Sepracor, Inc., USA

SO PCT Int. Appl., 34 pp.

Searcher : Shears 308-4994

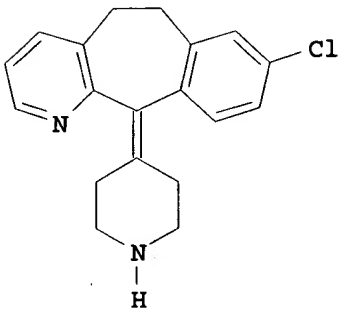


CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9834614	A1	19980813	WO 98-US2328	19980206
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9862719	A1	19980826	AU 98-62719	19980206

PRAI US 97-37325 19970207
US 97-45184 19970430
US 97-53050 19970721
WO 98-US2328 19980206

GI



I

AB Stable pharmaceutical compns. of descarboethoxyloratadine (DCL) (I), a metabolic deriv. of loratadine, for the treatment of allergic rhinitis and other histamine-induced disorders are disclosed. The compns. are formulated to avoid the incompatibility between I and reactive excipients such as lactose and other mono- and di-saccharides. Tablets were prepd. contg. I 10, starch 60, talc 12, acacia 12, and stearic acid 1 mg/tablet.

L60 ANSWER 2 OF 39 CAPLUS COPYRIGHT 1998 ACS
AN 1998:672493 CAPLUS

DN 129:281025
TI Chemically and thermally stable norastemizole formulations
IN Redmon, Martin P.; **Butler, Hal T.; Wald, Stephen A.**
PA Sepracor Inc., USA
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9842379	A2	19981001	WO 98-US5701	19980325

W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GW, HU, ID, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

PRAI US 97-824477 19970326
US 97-851786 19970506
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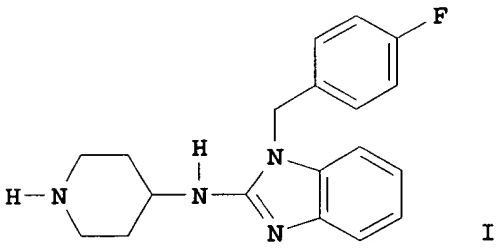


I

AB The present invention relates to chem. and thermally stable pharmaceutical formulations of the potent antihistamine, norastemizole (I). The compns. are lactose-free, non-hygroscopic, or anhyd., or comprise large particles or inertly coated I, or a pharmaceutically acceptable salt thereof, and are stable and easily manufd. A capsule compn. was prepd. contg. I 2.5, microcryst. cellulose 90.0, pregelatinized starch 100.3, croscarmellose 7.0, and Mg stearate 0.2 mg/capsule.

L60 ANSWER 3 OF 39 TOXLIT
AN 1998:131320 TOXLIT
DN CA-129-281025F

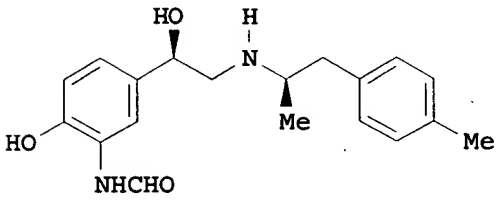
TI Chemically and thermally stable norastemizole formulations.
AU Redmon MP; **Butler HT**; **Wald SA**
SO (1998). PCT Int. Appl. PATENT NO. 9842379 10/01/1998 (Sepracor Inc.).
CODEN: PIXXD2.
CY UNITED STATES
DT Patent
FS CA
LA English
OS CA 129:281025
EM 199811
AB The present invention relates to chem. and thermally stable pharmaceutical formulations of the potent antihistamine, norastemizole (I). The compns. are lactose-free, non-hygroscopic, or anhyd., or comprise large particles or inertly coated I, or a pharmaceutically acceptable salt thereof, and are stable and easily manufd. A capsule compn. was prepd. contg. I 2.5, microcryst. cellulose 90.0, pregelatinized starch 100.3, croscarmellose 7.0, and Mg stearate 0.2 mg/capsule.

L60 ANSWER 4 OF 39 TOXLIT
AN 1998:111567 TOXLIT
DN CA-129-180143N
TI Lactose-free, non-hygroscopic and anhydrous pharmaceutical compositions of descarboethoxyloratadine.
AU Redmon MP; **Butler HT**; **Wald SA**; Rubin PD
SO (1998). PCT Int. Appl. PATENT NO. 9834614 08/13/1998 (Sepracor, Inc.).
CODEN: PIXXD2.
CY UNITED STATES
DT Patent
FS CA
LA English
OS CA 129:180143
EM 199809
AB Stable pharmaceutical compns. of descarboethoxyloratadine (DCL) (I), a metabolic deriv. of loratadine, for the treatment of allergic rhinitis and other histamine-induced disorders are disclosed. The compns. are formulated to avoid the incompatibility between I and reactive excipients such as lactose and other mono- and di-saccharides. Tablets were prepd. contg. I 10, starch 60, talc 12, acacia 12, and stearic acid 1 mg/tablet.

L60 ANSWER 5 OF 39 SCISEARCH COPYRIGHT 1998 ISI (R)
AN 97:637807 SCISEARCH
GA The Genuine Article (R) Number: XG123
TI D-fenfluramine-induced depletion of rat brain 5-HT is prevented by sibutramine or **fluoxetine** pretreatment.
AU Aspley S (Reprint); **Butler S A**; Prow M R; Martin K F; Heal

D J
CS KNOLL PHARMACEUT RES & DEV, NOTTINGHAM NG1 1GF, ENGLAND
CYA ENGLAND
SO DIABETOLOGIA, (JUN 1997) Vol. 40, Supp. [1], pp. 1470-1470.
Publisher: SPRINGER VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010.
ISSN: 0012-186X.
DT Conference; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 0

L60 ANSWER 6 OF 39 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 2
AN 1997:142812 CAPLUS
DN 126:250969
TI Enantioselective and diastereoselective synthesis of all four stereoisomers of formoterol
AU Hett, Robert; Fang, Qun Kevin; Gao, Yun; Hong, Yaping; **Butler, Hal T.**; Nie, Xiaoyi; **Wald, Stephen A.**
CS Sepracor Inc., Marlborough, MA, 01752, USA
SO Tetrahedron Lett. (1997), 38(7), 1125-1128
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier
DT Journal
LA English
OS CASREACT 126:250969
GI



I

AB The enantioselective synthesis of all four stereoisomers of formoterol was accomplished using asym. catalytic borane redns. with chiral oxazaborolidines as reducing agents. One of the target compds. was the L-tartrate salt of (R,R)-formoterol (I).

L60 ANSWER 7 OF 39 BIOSIS COPYRIGHT 1998 BIOSIS
AN 1997:371750 BIOSIS
DN PREV199799670953
TI D-fenfluramine-induced depletion of rat brain 5-HT is prevented by sibutramine or **fluoxetine** pretreatment.

AU Aspley, S.; **Butler, S. A.**; Prow, M. R.; Martin, K. F.; Heal, D. J.
CS Knoll Pharmaceuticals Res. Dev., Nottingham NG1 1GF UK
SO Diabetologia, (1997) Vol. 40, No. SUPPL. 1, pp. A374.
Meeting Info.: 16th International Diabetes Federation Congress Helsinki, Finland July 20-25, 1997
ISSN: 0012-186X.
DT Conference; Abstract; Conference
LA English

L60 ANSWER 8 OF 39 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 3
AN 1997:242257 BIOSIS
DN PREV199799541460
TI D-Fenfluramine-induced depletion of rat brain 5-HT is prevented by **fluoxetine** or sibutramine pretreatment.
AU **Butler, S. A.**; Slater, N. A.; Prow, M. R.; Aspley, S.; Martin, K. F.; Heal, D. J.
CS CNS Biology, Knoll Pharmaceuticals Res. Development, Nottingham NG1 1GF UK
SO British Journal of Pharmacology, (1997) Vol. 120, No. PROC. SUPPL., pp. 350P.
Meeting Info.: Meeting of the British Pharmacological Society Glaxo, Scotland December 18-20, 1996
ISSN: 0007-1188.
DT Conference; Abstract; Conference
LA English

L60 ANSWER 9 OF 39 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.
AN 1998073715 EMBASE
TI Mood disorders in the female patient.
AU **Redmond G.**
CS Dr. G. Redmond, Women's Hormone Center, 23200 Chagrin Boulevard, Beachwood, OH 44122, United States
SO International Journal of Fertility and Women's Medicine, (1997) 42/2 (67-72).
Refs: 5
ISSN: 1069-3130 CODEN: IJWMFW
CY United States
DT Journal; General Review
FS 010 Obstetrics and Gynecology
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Disruptive changes in mood and low energy level are among the most common reasons women consult a physician. Usually no clear physiological explanation for these changes can be found. Many physicians feel uncomfortable dealing with patients with these

complaints. The purpose of this paper is to discuss a practical approach to helping women with such conditions. A variety of terms have been utilized to refer to the situation in which a female patient has decreased energy or labile mood. Premenstrual Syndrome (PMS) and chronic fatigue syndrome (CFS) are currently popular terms. An association of low mood with menstrual cycle phase is undoubted, with the late luteal-early premenstrual phase most commonly associated with depression and irritability. It seems likely that women with PMS and those without it do not differ in circulating hormone levels during their cycles but rather in the brain response to these. Estrogen and progesterone receptors exist in the brain and change during the cycle. Elaborate diagnostic efforts are rarely rewarding in managing mood and energy disorders. Of more value is a careful history particularly concerned with the pattern of mood changes and with life stresses, accompanied by a thorough physical examination and laboratory tests. In most cases, changes in mood and energy are a variant of clinical depression. Changes in energy and sleep may be more evident than low affect. Treatment with an appropriate antidepressant, usually a selective serotonin re-uptake inhibitor (SSRI), benefits most of these patients. Allowing the patient to express concerns about stressful life situations is often of great value.

L60 ANSWER 10 OF 39 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 4
AN 1998:108253 BIOSIS
DN PREV199800108253
TI Monitoring of finger movements and hand muscle EMGs during mechanically perturbed writing tasks.
AU Bush, B. H. M. (1); **Butler, D. (1)**; **Redmond, N. M. (1)**; Westphely, H. (1); Whitlock, T.; Bateman, A.
CS (1) Univ. Bristol Dep. Physiol., Southwell St., Bristol BS2 8EJ UK
SO Journal of Physiology (Cambridge), (Nov., 1997) Vol. 504P, pp. 63P-64P.
Meeting Info.: Scientific Meetings of the Physiological Society Bristol, England, UK May 27-28, 1997 The Physiological Society . ISSN: 0022-3751.
DT Conference
LA English

L60 ANSWER 11 OF 39 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.
AN 1998146650 EMBASE
TI Late-life depression: Treatment strategies for primary care practice.
AU **Butler R.N.**; Cohen G.; Lewis M.I.; Simmons-Clemmons W.; Sunderland T.
CS Dr. R.N. Butler, International Longevity Center, Geriatrics/Adult Development Dept., Mount Sinai Medical Center, New York, NY, United States
SO Geriatrics, (1997) 52/4 (51-64).

Refs: 10
ISSN: 0016-867X CODEN: GERIAZ
CY United States
DT Journal; General Review
FS 020 Gerontology and Geriatrics
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Most patients age 65 and older with symptoms of depression respond well to treatment. Choices of therapy include medications, electroconvulsive therapy (ECT), and psychotherapy. Every primary care physician should be comfortable with using at least two or three medicines from different drug classes. The likelihood of side effects depends on the antidepressant prescribed and other medications the patient might be taking. The combination of medication with psychotherapy appears more effective than one or the other alone. ECT is the treatment of choice when rapid results are needed (eg, if the patient is suicidal or losing weight quickly and in danger of a medical crisis). The physician/patient relationship can be a strong antidepressant.

L60 ANSWER 12 OF 39 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 97-37814 DRUGU P
TI D-fenfluramine-induced depletion of rat brain 5-HT is prevented by sibutramine or **fluoxetine** pretreatment.
AU Aspley S; **Butler S A**; Prow M R; Martin K F; Heal D J
CS Knoll
LO Nottingham, U.K.
SO Diabetologia (40, Suppl. 1, A374, 1997) 1 Tab.
CODEN: DBTGAJ ISSN: 0012-186X
AV Knoll Pharmaceuticals Research and Development, Nottingham, NG1 1GF, England.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 97-37814 DRUGU P
AB Sibutramine (SIB) is a serotonin (5-HT) and noradrenaline reuptake inhibitor, and weight-loss agent. Weight-reducers which release 5-HT, viz. fenfluramine (d-fenfluramine; dFEN), cause profound brain 5-HT depletion in both rodents and non-human primates. The effects of p.o. dFEN with those of p.o. SIB and the selective serotonin reuptake inhibitor, i.p. **fluoxetine** (FLU) on rat brain 5-HT were compared. dFEN decreased 5-HT levels but FLU and SIB had no effect. The results confirm that dFEN persistently depletes brain 5-HT, but the monoamine reuptake inhibitors, SIB and FLU do not. Taken together with evidence from microdialysis studies

which show SIB and FLU inhibited, dFEN from releasing 5-HT, the data suggested that SIB and FLU prevent the 5-HT depleting effects of dFEN by blocking its entry into 5-HT nerve terminals. (conference abstract).

ABEX Methods Male SD rats (80 - 100 g) received vehicle, dFEN 10 mg/kg p.o., SIB 9 mg/kg p.o. or FLU 10 mg/kg i.p. for 4 days, b.i.d., alone or in combination (SIB or FLU 1 h prior to dFEN); 14 days later, brain tissue 5-HT content was determined by HPLC-ED. Results dFEN decreased 5-HT levels in all regions. In striking contrast, FLU and SIB did not alter brain 5-HT levels and actually prevented the dFEN-induced decreases in 5-HT in the majority of areas. In the frontal cortex, hippocampus, striatum and hypothalamus, respectively, FLU levels were 513, 446, 596, and 912; dFEN levels were 176, 151, 250, and 673; FLU/dFEN levels were 507, 448, 534, and 873; SIB were 644, 552, 346 and 756; dFEN were 234, 214, 220, and 579; and SIB/dFEN were 534, 480, 354 and 704. (LG)

L60 ANSWER 13 OF 39 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 5
AN 1997:49398 BIOSIS
DN PREV199799348601
TI Effect of the selective 5-HT-1B/1D receptor antagonist, GR127935, in combination with **fluoxetine** on rat brain 5-hydroxytryptophan levels.
AU Spencer, E. L.; **Butler, S. A.**; Slater, N. A.; Aspley, S.; Cheetham, S. C.; Martin, K. F.; Heal, D. J.
CS Knoll Pharm. Res. Development, Nottingham NG2 3AA UK
SO British Journal of Pharmacology, (1996) Vol. 119, No. PROC. SUPPL., pp. 183P.
Meeting Info.: Joint Meeting of the British Pharmacological Society, the Pharmacological Society of Canada and the Canadian Society for Clinical Pharmacology Bath, England, UK July 10-12, 1996
ISSN: 0007-1188.
DT Conference; Abstract; Conference
LA English

L60 ANSWER 14 OF 39 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 6
AN 1996:137223 CAPLUS
DN 124:250580
TI [3H]nisoxetine - a radioligand for noradrenaline reuptake sites: correlation with inhibition of [3H]noradrenaline uptake and effect of DSP-4 lesioning and antidepressant treatments
AU Cheetham, S. C.; Viggers, J. A.; **Butler, S. A.**; Prow, M. R.; Heal, J.
CS Res. Dep., Knoll Pharmaceuticals, Nottingham, NG2 3AA, UK
SO Neuropharmacology (1996), 35(1), 63-70
CODEN: NEPHBW; ISSN: 0028-3908
DT Journal
LA English
AB Nisoxetine is a potent and selective inhibitor of noradrenaline

uptake into noradrenergic neurons. [3H]nisoxetine binding to rat frontal cortical membranes was of high affinity. The binding data of both competition and satn. studies fitted a single site binding model. [3H]nisoxetine binding was potently inhibited by the selective noradrenaline uptake inhibitors desipramine and protriptyline. In addn., a very good correlation was obtained between the ability of 25 monoamine reuptake inhibitors and related compds. both to inhibit [3H]nisoxetine binding and to inhibit [3H]noradrenaline uptake in rat frontal cortex. DSP-4 (10-100 mg/kg, i.p.) dose-dependently depleted cortical noradrenaline concns. (51-100%0), with no significant effects on 5-HT and dopamine. These depletions, which are used as a marker of loss of noradrenergic nerve terminals, were assocd. with a dose-dependent decrease in the no. of [3H]nisoxetine binding sites (20-97%) with no change in binding affinity. Furthermore, a good correlation was obtained between cortical noradrenaline concns. and the no. of [3H]nisoxetine binding sites. These data support the view that [3H]nisoxetine binds to a single population of homogeneous sites assocd. with the noradrenaline transporter complex. Using this ligand, the effects of repeated administration of both antidepressant drugs with a range of pharmacol. actions and of electroconvulsive shock on noradrenaline reuptake sites were examd. The no. and affinity of [3H]nisoxetine binding sites were unaltered by all treatments. It is unlikely, therefore, that antidepressant therapy would produce adaptive changes in noradrenaline uptake sites.

L60 ANSWER 15 OF 39 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 7
AN 1996:197404 BIOSIS
DN PREV199698753533
TI Albuterol: A pharmaceutical chemistry review of R-, S-, and RS-albuterol.
AU Bakale, Roger P. (1); **Wald, Stephen A.**; **Butler, Hal T.**; Gao, Yun; Hong, Yaping; Nie, Xiaoyi; Zepp, Charles M.
CS (1) Sepracor Inc., 33 Locke Drive, Marlborough, MA 01752 USA
SO Clinical Reviews in Allergy & Immunology, (1996) Vol. 14, No. 1, pp. 7-35.
ISSN: 1080-0549.
DT General Review
LA English

L60 ANSWER 16 OF 39 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.DUPLICATE 8
AN 95247187 EMBASE
TI Late-life depression: When and how to intervene.
AU **Butler R.N.**; Lewis M.I.
CS Geriatrics/Adult Development Dept., Mount Sinai Medical Center, New York, NY, United States
SO Geriatrics, (1995) 50/8 (44-55).

ISSN: 0016-867X CODEN: GERIAZ
CY United States
DT Journal
FS 020 Gerontology and Geriatrics
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Late-life depression ranges from mild to severe and can lead to significant physical and social limitations. Up to one-third of patients with medical disorders also suffer from depressive symptoms. Differential diagnosis of depression is often confounded by medical conditions that impair cognitive functioning, such as Alzheimer's disease and vascular dementia. Depression is a modifiable risk factor for suicide in old age. Once diagnosed, depression is a highly treatable disease. Treatment modalities include psychotherapy, antidepressants, and electroconvulsive therapy for intractable cases. Many patients are now being treated in primary care settings, due to managed care limits on referrals and to patient reluctance to seek psychiatric care.

L60 ANSWER 17 OF 39 EMBASE
AN 95179197 EMBASE
TI Older women's health: Clinical care in the postmenopausal years. A roundtable discussion: Part 2.
AU **Butler R.N.**; Collins K.S.; Meier D.E.; Muller C.F.; Pinn V.W.
CS International Longevity Ctr. (U.S.), New York, NY, United States
SO Geriatrics, (1995) 50/6 (33+36+39-41).
ISSN: 0016-867X CODEN: GERIAZ
CY United States
DT Journal
FS 020 Gerontology and Geriatrics
032 Psychiatry
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Prevention of late-life disability is an important goal in managing the health care of older women. Hormone replacement therapy and regular exercise can protect against osteoporosis and heart disease. Dietary measures can control weight and prevent diabetes. Adequate calcium and vitamin D intake help protect bones from fractures. Mammography and Pap smears are proven screens for early cancer detection. Depression is not unusual in older women, but it is often masked by physical symptoms. Physicians can help women at risk for caregiver burnout by providing referrals and information on

community resources. Use of other health professionals, as well as patient education videos and printed materials, can help physicians provide comprehensive care within the time limits of office practice.

L60 ANSWER 18 OF 39 CAPLUS COPYRIGHT 1998 ACS
AN 1994:446960 CAPLUS
DN 121:46960
TI Preparation and spectroscopic characterization of highly confined nanocrystallites of gallium arsenide in decane. [Erratum to document cited in CA119(20):214190m]
AU **Butler, Liam**; **Redmond, Gareth**; Fitzmaurice, Donald
CS Dep. Chem., Univ. Coll. Dublin, Dublin, Ire.
SO J. Phys. Chem. (1994), 98(17), 4772
CODEN: JPCHAX; ISSN: 0022-3654
DT Journal
LA English
OS CJACS
AB The errors were not reflected in the abstr. or the index entries.

L60 ANSWER 19 OF 39 SCISEARCH COPYRIGHT 1998 ISI (R)
AN 94:294914 SCISEARCH
GA The Genuine Article (R) Number: NJ538
TI PREPARATION AND SPECTROSCOPIC CHARACTERIZATION OF HIGHLY CONFINED NANOCRYSTALLITES OF GAAS IN DECANE (VOL 97, PG 10750, 1993)
AU **BUTLER L (Reprint)**; **REDMOND G**; FITZMAURICE D
SO JOURNAL OF PHYSICAL CHEMISTRY, (28 APR 1994) Vol. 98, No. 17, pp. 4772.
ISSN: 0022-3654.
DT Errata; Journal
FS PHYS
LA ENGLISH
REC Reference Count: 3

L60 ANSWER 20 OF 39 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 94-22222 DRUGU P
TI (3H)Nisoxetine, a novel ligand for noradrenaline (NA) uptake sites: correlations with inhibition of (3H)NA uptake and loss of NA nerve terminals after denervation.
AU Cheetham S C; Viggers J A; **Butler S A**; Prow M R; Heal D J
CS Boots
LO Nottingham, United Kingdom
SO Br.J.Pharmacol. (112, Proc.Suppl., 156P, 1994) 1 Tab. 3 Ref.
CODEN: BJPCBM ISSN: 0007-1188
AV Boots Pharmaceuticals Research Department, Nottingham NG2 3AA, England.
LA English
DT Journal

FA AB; LA; CT; MPC
FS Literature
AN 94-22222 DRUGU P
AB 3H-nisoxetine (NI) binding in rat frontal cortical membranes and synaptosomes (defined by mazindol and desipramine) was inhibited by varying degrees by desipramine, protriptyline, nomifensine, doxepin, maprotiline, amitriptyline, imipramine, clomipramine, dothiepin, mianserin, **fluoxetine** and fluvoxamine, respectively. A good correlation was obtained between the potency of antidepressants to inhibit 3H-NI binding and 3H-noradrenaline (NA) uptake. I.p. DSP-4 administered to rats 30 min after i.p. zimeldine depleted cortical NA concentrations and decreased the number of 3H-NI binding sites. Results indicate that 3H-NI binds to a single population of homogenous sites associated with the NA transporter complex. (congress abstract).
ABEX Ki values for 3H-NI (1 nM) binding in rat frontal cortical membranes and synaptosomes defined by mazindol (1 uM) and desipramine (10 uM), respectively) were 1.6, 6.2, 25, 24, 20, 23, 29, 52, 67, 130, 902 and 1761 for desipramine, protriptyline, nomifensine, doxepin, maprotiline, amitriptyline, imipramine, clomipramine, dothiepin, mianserin, **fluoxetine** and fluvoxamine, respectively. Corresponding values for 3H-NA (10 nM) uptake were 1.7, 2.5, 8, 18, 26, 28, 29, 40, 70, 87, 320 and 612. 3H-NI binding to rat cortex was of high affinity. A good correlation was obtained between the potency of antidepressants to inhibit 3H-NI binding and 3H-NA uptake. I.p. DSP-4 (10, 20, 50 and 100 mg/kg) administered to rats 30 min after i.p. zimeldine (10 mg/kg) dose-dependently depleted cortical NA concentrations by 51%, 73%, 100% and 100%, respectively. These depletions were associated with a dose-dependent decrease in the number of 3H-NI binding sites by 20%, 49%, 86% and 97%, with no change in binding affinity. A good correlation was obtained between cortical NA concentrations and the number of 3H-NI binding sites. (JE)

L60 ANSWER 21 OF 39 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.
AN 94032049 EMBASE
TI Vascular dementia: An updated approach to patient management.
AU **Butler R.N.**; Ahronheim J.; Fillit H.; Rapoport S.I.; Tatemichi T.K.
CS Geriatrics/Adult Development Dept., Mount Sinai School of Medicine, New York, NY, United States
SO GERIATRICS, (1994) 49/1 (39-46).
ISSN: 0016-867X CODEN: GERIAZ
CY United States
DT Journal
FS 006 Internal Medicine
008 Neurology and Neurosurgery
020 Gerontology and Geriatrics
037 Drug Literature Index

LA English
SL English
AB A new clinical approach to the prevention and treatment of vascular dementia is evolving. The physician has numerous options to consider when the patient is in an asymptomatic 'brain at risk' stage. These include treatment of hypertension, elevated cholesterol, and atrial fibrillation, as well as smoking cessation, exercise, and dietary changes. When there are early signs of cerebrovascular disease, such as TIAs and subtle cognitive changes, more aggresssive therapy may be warranted, including carotid endarterectomy, anticoagulants, aspirin, and ticlopidine. For patients with vascular dementia, treatment focuses on preventing further cerebrovascular damage and managing related symptoms, such as depression.

L60 ANSWER 22 OF 39 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 9
AN 1993:614190 CAPLUS
DN 119:214190
TI Preparation and spectroscopic characterization of highly confined nanocrystallites of gallium arsenide in decane
AU **Butler, Liam**; **Redmond, Gareth**; Fitzmaurice, Donald
CS Dep. Chem., Univ. Coll. Dublin, Dublin, Ire.
SO J. Phys. Chem. (1993), 97(41), 10750-5
CODEN: JPCHAX; ISSN: 0022-3654
DT Journal
LA English
OS CJACS
AB GaAs nanocrystallites were prepd. by refluxing GaCl3 with As(SiMe3)3 in decane at 180.degree. for 72 h. The crystallites formed have an av. diam. of 3 nm. Controlled growth of these crystallites to a desired av. diam. is possible by autoclaving at 200.degree.. Changes in the measured optical absorption spectrum assocd. with this ripening process are described. Spectral features in the 400-550-nm region, previously assigned to mol. species in soln. or adsorbed at the surface of GaAs crystallites, are absent. Optical absorption bands at 302 and 314 nm, obsd. for GaAs crystallites whose av. diams. are 3 and 4 nm, resp., are tentatively assigned to the 1S-1S transition. The obsd. absorption onset is compared with that predicted, using the effective mass approxn. and pseudopotential methods, for spherical crystallites of the appropriate diam. Agreement of the measured onset for absorption with that predicted from the effective mass approxn. is excellent. However, for crystallites whose diam. is .ltorsim.5 nm the obsd. blue shift is smaller than predicted. Implications of these observations are discussed.

L60 ANSWER 23 OF 39 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 10
AN 1994:452 CAPLUS
DN 120:452

TI Chronic electroconvulsive seizures increase the expression serotonin2 receptor mRNA in rat frontal cortex

AU **Butler, Marcus O.**; Morinobu, Shigeru; Duman, Ronald S.
CS Sch. Med., Yale Univ., New Haven, CT, 06508, USA

SO J. Neurochem. (1993), 61(4), 1270-6
CODEN: JONRA9; ISSN: 0022-3042
DT Journal
LA English

AB The present study examines the influence of electroconvulsive seizure (ECS), as well as antidepressant drugs, on levels of serotonin2 (5-HT2) receptor mRNA in rat frontal cortex. Using a sensitive RNAse protective assay, preliminary studies demonstrated the predicted regional distribution for the 5-HT2 receptor mRNA: levels of 5-HT2 mRNA were highest in frontal cortex (2.58 mol/.mu.g of total RNA), intermediate in neostriatum, thalamus, and midbrain, and lowest in hippocampus, cerebellum, and choroid plexus. Chronic (10 or 14 days), but not acute (1 or 3 days), ECS treatment significantly increased levels of 5-HT2 receptor mRNA. ECS treatment resulted in a similar time-dependent up-regulation of 5-HT2 receptor ligand binding; chronic, but not acute, ECS treatment significantly increased levels of [3H]ketanserin ligand binding, confirming previous reports. Northern blot anal. demonstrated that 5-HT2 receptor mRNA occurs as two bands (.apprx.5 and 6 kb in size), both of which were increased by chronic ECS treatment. The influence of antidepressant drug treatments on 5-HT2 receptor mRNA was also examd. Chronic **fluoxetine** treatment increased levels of 5-HT2 receptor mRNA, although levels of [3H]ketanserin ligand binding were not altered. In contrast, chronic administration of imipramine, mianserin, and tranylcypromine, treatments that decreased ligand binding, did not decrease levels of 5-HT2 receptor mRNA. In fact, mianserin treatment caused a small, but significant, increase in levels of receptor mRNA. The results suggest that ECS up-regulation of 5-HT2 receptor mRNA could underlie the increased d. of 5-HT2 receptor binding sites in response to this treatment, but that other mechanisms likely operate in the downregulation of 5-HT2 receptor ligand binding by antidepressant drug treatments.

L60 ANSWER 24 OF 39 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 11
AN 1993:596099 CAPLUS
DN 119:196099
TI The effect of modulation of central serotonin neurotransmission on osmoregulated vasopressin release in rats
AU Faull, C. M.; Charlton, J. A.; Phillips, E.; Thornton, S.; **Butler, T.**; Baylis, P. H.
CS Med. Sch., Univ. Newcastle-upon-Tyne, Newcastle-upon-Tyne, NE2 4HH, UK
SO Ann. N. Y. Acad. Sci. (1993), 689(Neurohypophysis: A Window on Brain Function), 484-8

CODEN: ANYAA9; ISSN: 0077-8923
DT Journal
LA English
AB Acute administration of the selective serotoninergic reuptake inhibitor **fluoxetine** to rats increased basal AVP secretion and increased the sensitivity of the AVP response to changes in plasma osmolality. Chronic **fluoxetine** treatment decreased the sensitivity of AVP release to plasma osmolality without affecting osmolality. Chronic **fluoxetine** treatment also decreased the hematocrit values.

L60 ANSWER 25 OF 39 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 12
AN 1994:24178 CAPLUS
DN 120:24178
TI The effect of acute pharmacological manipulation of central serotonin neurotransmission on osmoregulated secretion of arginine vasopressin in the rat
AU Faull, C. M.; Charlton, J. A.; **Butler, T. J.**; Baylis, P. H.
CS Dep. Med. Medical School, Univ. Newcastle upon Tyne, Newcastle upon Tyne, NE2 4HH, UK
SO J. Endocrinol. (1993), 139(1), 77-87
CODEN: JOENAK; ISSN: 0022-0795
DT Journal
LA English
AB To explore the hypothesis that serotonin (5-HT) is important in osmoregulated arginine vasopressin (AVP) secretion, the authors administered (i.p.) **fluoxetine** (FL) a 5-HT reuptake inhibitor (10 mg/kg body wt.), ritanserin (RIT), an antagonist at the 5-HT2 and 5-HT1c receptor subtypes (1 mg/kg body wt.), 1-(4-iodo-2,5-dimethoxyphenyl)-2-aminopropane hydrochloride (DOI), a 5-HT2 receptor agonist (1 mg/kg body wt) or vehicle to rats 30 min before they were given an osmotic challenge. Rats received distd. water, normotonic saline (150 mmol NaCl/L) or hypertonic saline (500 mmol NaCl/L) (20 mL/kg i.p.) and were killed 30 min later. The osmotic stimulus alone produced significant effects on plasma osmolality and plasma sodium but FL, RIT and DOI did not have any significant effect on this stimulus. FL had no significant effect on the osmotic threshold of AVP release but significantly increased basal AVP secretion from 1.6 to 3.1 pmol AVP/L and significantly increased the AVP response to changes in plasma osmolality: vehicle-treated, 0.7; FL-treated, 1.7 pmol AVP/L per mOsm per kg. Neither RIT nor DOI had any significant effect on basal or stimulated AVP secretion. In a second study, RIT was administered 60 min i.p. prior to FL i.p. (doses as above), which was followed 30 min later by a hypertonic stimulus i.p. and rats were killed 30 min after hypertonic saline treatment. RIT had no significant effect on the AVP response to plasma osmolality and did not significantly alter the FL-augmented AVP response, suggesting that neither the

5-HT2 nor the 5-HT1c receptors are involved in the response to AVP to FL. The authors conclude that FL modulates osmoregulated AVP secretion but that the mechanism of this is unknown and is apparently not through the 5-HT2 or 5-HT1c receptor subtypes.

L60 ANSWER 26 OF 39 SCISEARCH COPYRIGHT 1998 ISI (R)
AN 92:578399 SCISEARCH
GA The Genuine Article (R) Number: JQ520
TI ANTENATAL SCREENING FOR DOWNS-SYNDROME
AU **WALD N J (Reprint)**; KENNARD A; DENSEM J W; CHARD T; **BUTLER L**
CS ST BARTHOLOMEWS HOSP, COLL MED, WOLFSON INST PREVENT MED, DEPT ENVIRONM & PREVENT MED, LONDON EC1M 6BQ, ENGLAND (Reprint); ST BARTHOLOMEWS HOSP, COLL MED, DEPT REPROD PHYSIOL, LONDON EC1M 6BQ, ENGLAND; QUEEN ELIZABETH HOSP CHILDREN, N E THAMES REG CYTOGENET LAB, LONDON E2 8PS, ENGLAND
CYA ENGLAND
SO BRITISH MEDICAL JOURNAL, (26 SEP 1992) Vol. 305, No. 6856, pp. 771. ISSN: 0959-8138.
DT Letter; Journal
FS LIFE; CLIN
LA ENGLISH
REC Reference Count: 9

L60 ANSWER 27 OF 39 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 13
AN 1992:460583 BIOSIS
DN BA94:101983
TI ANTENATAL MATERNAL SERUM SCREENING FOR DOWN'S SYNDROME RESULTS OF A DEMONSTRATION PROJECT.
AU **WALD N J**; KENNARD A; DENSEM J W; CUCKLE H S; CHARD T; **BUTLER L**
CS DEP. ENVIRONMENTAL PREVENTIVE MEDICINE, WOLFSON INSTITUTE PREVENTIVE MEDICINE, MEDICAL COLLEGE ST. BARTHOLOMEW'S HOSPITAL, LONDON EC1M 6BQ.
SO BR MED J, (1992) 305 (6850), 391-394.
CODEN: BMJOAE. ISSN: 0007-1447.
FS BA; OLD
LA English
AB Objective: To assess the implementation of antenatal screening for Down's syndrome in practice, using individual risk estimates based on maternal age and the three serum markers: .alpha. fetoprotein, unconjugated oestriol, and human chorionic gonadotrophin. Design: Demonstration project of Down's syndrome screening; women with a risk estimate at term of 1 in 250 or greater were classified as "screen positive" and offered diagnostic amniocentesis. Setting: Hospital and community antenatal clinics in four health districts in London. Subjects: 12603 women of all ages with singleton pregnancies seen between February 1989 and the end of May 1991, with follow up of the outcome of pregnancy completed to the end of 1991.

Main outcome measures: Uptake of screening, detection rate for Down's syndrome, false positive rate, odds of being affected given a positive result, and uptake of amniocentesis in women with positive screening results, together with the costs of the screening programme. Results: The uptake of screening was 74%. The detection rate was 48% (12/25), and the false positive rate was 4.1%, consistent with results expected from previous work based on observational studies. There was a loss of detection due to the selective use of ultrasound scans among women with positive screening results. One affected pregnancy occurred among 205 reclassified as negative; this illustrated the danger of false negatives occurring in this group and lends weight to the view that if an ultrasound estimate of gestational age is used it should be carried out routinely on all women rather than selectively among those with positive results. The estimated cost of avoiding the birth of a baby with Down's syndrome was about .pnd.38 000, substantially less than the lifetime costs of care. Conclusion: Antenatal maternal serum screening for Down's syndrome is effective in practice and can be readily integrated into routine antenatal care. It is cost effective and performs better than selection for amniocentesis on the basis of maternal age alone.

L60 ANSWER 28 OF 39 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.
AN 92174288 EMBASE
TI Aging and mental health: Primary care of the healthy older adult.
AU **Butler R.N.**; Finkel S.I.; Lewis M.I.; Sherman F.T.; Sunderland T.
CS Dept. of Geriatrics and Adult Devt., Mount Sinai Medical School, New York, NY, United States
SO GERIATRICS, (1992) 47/5 (54+56+61-65).
ISSN: 0016-867X CODEN: GERIAZ
CY United States
DT Journal
FS 020 Gerontology and Geriatrics
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Dementia, depression, alcoholism, and suicide are some of the most important mental health issues for the aging population. Among the factors that affect the physician's ability to evaluate and manage these disorders are drug-induced side effects, the ability and willingness of patients to communicate their feelings, the level of caregiver cooperation, and limitations imposed by federal regulations and reimbursement policies. In this first of three installments of a panel discussion, experts in geriatrics and geropsychiatry discuss healthy aging, age-related memory and sensory loss, changes in mentation postanesthesia, sexuality in the elderly,

and side effects of common psychoactive medications.

L60 ANSWER 29 OF 39 MEDLINE DUPLICATE 14
AN 90237429 MEDLINE
DN 90237429
TI Clinical and experimental studies on **fluoxetine**: effects on serotonin uptake.
AU **Butler J**; Leonard B E
CS Department of Pharmacology, University College, Galway, Ireland.
SO INTERNATIONAL CLINICAL PSYCHOPHARMACOLOGY, (1990 Jan) 5 (1) 41-8. Journal code: ICP. ISSN: 0268-1315.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199008
AB A decreased rate of uptake of serotonin (5HT) into platelets is recognized as a possible marker of the depressed state, being normalized only by effective antidepressant treatment. **Fluoxetine** is a novel antidepressant, with 5HT uptake inhibitory properties. In this study, treatment of depressed patients with **fluoxetine** for up to 6 months did not normalize the decreased platelet 5HT uptake rates associated with depression, although the patients showed a clinical recovery. The olfactory bulbectomized (OB) rat shows a characteristic hyperactivity in a stressful environment, which can be reversed only by chronic treatment with most antidepressants. OB rats have been found to exhibit a decreased rate of platelet 5HT uptake, similar to depressed patients, which is normalized by chronic antidepressant treatment. However, 3 weeks treatment with **fluoxetine** failed to reverse the hyperactivity of the OB rat and the decreased rates of uptake of 5HT. We also examined the rate of uptake of serotonin into the synaptosomes of the OB rats, in order to elucidate whether platelet 5HT uptake reflected central activity. Chronic **fluoxetine** treatment failed to normalize high affinity synaptosomal 5HT uptake in the OB rat. **Fluoxetine** , therefore, unlike most other antidepressants, does not normalize the decreased rates of platelet 5HT uptake in depressed patients on clinical recovery. OB rats also showed a deficit in their platelet and synaptosomal 5HT uptake rates, following 3 weeks treatment with **fluoxetine**.

L60 ANSWER 30 OF 39 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 90-36293 DRUGU P
TI (3H)GR67330, a Very High Affinity Ligand for 5-HT3 Receptors.
AU Kilpatrick G J; **Butler A**; Hagan R M; Jones B J; Tyers M B
CS Glaxo
LO Ware, United Kingdom
SO Arch.Pharmacol. (342, No. 1, 22-30, 1990) 7 Fig. 3 Tab. 27 Ref.

CODEN: NSAPCC ISSN: 0028-1298
AV Dept. of Neuropharmacology, Glaxo Group Research Ltd., Ware, Herts, SG12 0DP, England.
LA English
DT Journal
FA AB; LA; CT; MPC
FS Literature
AN 90-36293 DRUGU P
AB GR-67330 (GR) potently antagonized 5-HT induced depolarization of rat vagus nerve in vitro. Specific 3H-GR binding to rat brain was inhibited by SDZ-206-830 HCl, BRL-43694 HCl, 2-methyl-5-HT, GR, GR-38032 HCl dihydrate, GR-65630 malate (all Glaxo), MDL-72222, ICS-205930 (both Research-Biochem.), zacopride HCl (Robins), 5-HT, metoclopramide HCl (ME, both Sigma-Chem.), m-chlorophenylpiperazine (mCPP), quipazine (QU, Miles), tubocurarine, phenylbiguanide, cocaine HCl (May+Baker), **fluoxetine**, imipramine and desipramine. Methiothepin malate (Roche), alpha-methyl-5-HT, 5-carboxyamidotryptamine malate (5-CT, both Glaxo), GABA, noradrenaline bitartrate, dopamine (all Sigma-Chem.), ACh, 8-OH-DPAT (Research-Biochem.), methysergide (Sandoz), ketanserin (Salford), diazepam (Evans), hexamethonium and melatonin were weak.

ABEX In the rat isolated vagus nerve, GR (0.1-10 nmol/l; pKB, 10.2) potently inhibited 5-HT (0.3-30 umol/l) induced depolarizations, accompanied by marked reduction in the maximum response to 5-HT at the higher concentrations (0.3-1 nmol/l). In homogenates of rat entorhinal cortex, specific 3H-GR binding (defined using ME) was rapid, reversible, readily saturable, and to a single site (Bmax, 22.6 fmol/mg protein) of high affinity (Kd, 0.038 nmol/l). The association rate constant was 1.47 mol/l/sec, dissociation rate constant was 7.85/10 power 3/sec), and affinity constant 0.053 nmol/l. Using unlabeled GR (10 umol/l) to define nonspecific binding, 2 sites were evident, (Kd 0.066 nmol/l, Bmax 31.5 fmol/mg protein; and Kd 20.1 nmol/l, Bmax 1110 fmol/mg protein). 3H-GR (0.1 nmol/l) binding was inhibited potently (up to 70% of total) by QU, ICS-205930, SDZ-206830, MDL-72222, BRL-43694, zacopride, cocaine, mCPP, tubocurarine, ME, 5-HT, 2-methyl-5-HT, and phenylbiguanide. GR, GR-38032, and GR-65630 inhibited up to 90% of total 3H-GR binding at high and low affinity sites. Methiothepin, alpha-methyl-5-HT, methysergide, noradrenaline, ACh, 8-OH-DPAT, ketanserin, 5-CT, GABA, diazepam, dopamine, melatonin, and hexamethonium were weak or inactive. **Fluoxetine**, imipramine, and desipramine were not potent inhibitors. A single high affinity specific 3H-GR binding site was detected in homogenates of rat entorhinal, cingulate, and parietal cortex, hippocampus, and nucleus accumbens/olfactory tubercle, with similar drug inhibition profiles (using zacopride, ICS-205930, BRL-43694, quipazine, 5-HT, and GR-38032). (E27/LJ)

AN 1990:129533 BIOSIS
DN BA89:68344
TI ULTRASOUND FETAL FEMUR LENGTH MEASUREMENT IN THE SCREENING FOR DOWN'S SYNDROME.
AU CUCKLE H; **WALD N**; QUINN J; ROYSTON P; **BUTLER L**
CS DEP. ENVIRON. AND PREVENTIVE MED., MED. COLL. ST. BARTHOLOMEW'S HOSP., CHARTERHOUSE SQUARE, LONDON EC1M 6BQ.
SO BR J OBSTET GYNAECOL, (1989) 96 (12), 1373-1378.
CODEN: BJOGAS. ISSN: 0306-5456.
FS BA; OLD
LA English
AB The fetal femur length determined by an ultrasound examination at between 13 and 39 weeks gestation in 83 pregnancies associated with Down's syndrome was statistically significantly less than the expected value for pregnancies with the same biparietal diameter examined in the same ultrasound department ($P < 0.0001$). Expected values were based on linear regressions of femur length on biparietal diameter in 1340 control pregnancies from 27 ultrasound department. The median value for the affected pregnancies was 0.94 times the expected value (95% CI 0.92 to 0.97). Eleven per cent of affected and 1.4% of control pregnancies had values .ltoreq. 0.85 times the expected. The reduction in femur length in affected pregnancies was not related to biparietal diameter or to maternal age. Fetal femur length may be useful as an ancillary screening variable in the antenatal screening for Down's syndrome.

L60 ANSWER 32 OF 39 BIOSIS COPYRIGHT 1998 BIOSIS
AN 1990:166018 BIOSIS
DN BR38:76806
TI AFFINITIES OF 5 HT UPTAKE INHIBITORS FOR 5 HT-3 RECEPTORS IN BOTH BINDING AND FUNCTIONAL STUDIES.
AU KILPATRICK G J; **BUTLER A**; IRELAND S J; MICHEL A D; TYERS M D
CS DEP. NEUROPHARMACOL., GLAXO GROUP RES. LTD., WARE, HERTS. SG12 0DP, UK.
SO MEETING OF THE BRITISH PHARMACOLOGICAL SOCIETY, MANCHESTER, ENGLAND, UK, SEPTEMBER 13-15, 1989. BR J PHARMACOL. (1989) 98 (PROC SUPPL DEC), 859P.
CODEN: BJPCBM. ISSN: 0007-1188.
DT Conference
FS BR; OLD
LA English

L60 ANSWER 33 OF 39 MEDLINE
AN 87001219 MEDLINE
DN 87001219
TI Compliance with screening for colorectal cancer [letter].
AU Cuckle H S; **Wald N J**; **Butler E B**
SO BRITISH MEDICAL JOURNAL (CLINICAL RESEARCH ED.), (1986 Sep 6) 293

(6547) 628.
Journal code: B4X. ISSN: 0267-0623.
CY ENGLAND: United Kingdom
DT Letter
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 198701

L60 ANSWER 34 OF 39 SCISEARCH COPYRIGHT 1998 ISI (R)
AN 86:498972 SCISEARCH
GA The Genuine Article (R) Number: D8679
TI COMPLIANCE WITH SCREENING FOR COLORECTAL-CANCER
AU CUCKLE H S (Reprint); **WALD N J**; **BUTLER E B**
CS ST BARTHOLOMEWS HOSP, COLL MED, DEPT ENVIRONM & PREVENT MED, LONDON EC1M 6BQ, ENGLAND (Reprint); ELIZABETH GARRETT ANDERSON HOSP, EARLY DIAGNOST UNIT, LONDON NW1 2AP, ENGLAND
CYA ENGLAND
SO BRITISH MEDICAL JOURNAL, (1986) Vol. 293, No. 6547, pp. 628.
DT Letter; Journal
FS LIFE; CLIN
LA ENGLISH
REC Reference Count: 3

L60 ANSWER 35 OF 39 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 85-08472 DRUGU C P S
TI (1,3-Dialkyl-5-amino 1H-pyrazol-4-yl) Arylmethanones. A Series of Novel Central Nervous System Depressants.
AU **Butler D E**; Wise L D; **Wald H A de**
CS Warner-Parke-Davis
LO Ann Arbor, Michigan, United States
SO J.Med.Chem. (27, No. 11, 1396-400, 1984) 2 Tab. 18 Ref.
CODEN: JMCMAR ISSN: 0022-2623
AV Warner-Lambert/Parke-Davis Pharmaceutical Research, Ann Arbor, Michigan 48106, U.S.A.
LA English
DT Journal
FA AB; LA; CT; MPC
FS Literature
AN 85-08472 DRUGU C P S
AB A series of (1,3-dialkyl-5-amino 1H-pyrazol-4-yl) arylmethanones was prepared and tested for CNS depressant activity (i.p. in mice) using pimozide and thioridazine as standards, and for anticonvulsant activity (p.o. in rats), using tridione, phensuximide, and methaqualone as standards. Compounds had low acute toxicity. Structure-activity relationships were evaluated.
ABEX Compounds (1-35) were prepared, confirmed by IR and NMR spectra. Behavioral tests in male albino mice (20-26 g) and antipentetrazole test in rats, showed that (21) had an anticonvulsant dose (16 mg/kg) at 50% of the central depressant dose (32 mg/kg). Compound

(12) at 8 mg/kg had depressant activity and was devoid of anticonvulsant activity. Compounds (8), (13) and (14) were potent depressants. In Swiss-Webster male mice (20-30 g), using the locomotion-screen fall off test, (2) showed a profile indicative of antipsychotic activity. (2) Gave a positive Ames test.

L60 ANSWER 36 OF 39 SCISEARCH COPYRIGHT 1998 ISI (R)
AN 84:500448 SCISEARCH
GA The Genuine Article (R) Number: TL561
TI AN INVESTIGATION OF NARROW MESON RESONANCE PRODUCTION IN ANTIPROTON PROTON AND ANTIPROTON NEUTRON INTERACTIONS AT 6.1 AND 8.9 GEV/C
AU AZOOZ F (Reprint); BUTTERWORTH I; DORNAN P J; HALL G; STERN R A; WHITE A P; BROWN R C; **BUTLER N**; GOPAL G P; MCPHERSON A; SEKULIN R L; BARLOUTAUD R; CAMBIER J L; LORET M; OKUSAWA T; STEVENS R; VILANOVA D; BRAU J E; CARROLL J T; CHALOUPKA V; CAUTIS C V; DUMONT J J; ERICSON R A; FIELD R C; FREYTAG D R; GRANDPEIX J Y; KITAGAKI T; TANAKA S; YUTA H; ABE K; HASEGAWA K; YAMAGUCHI A; TAMAI K; TAKANASHI H; MANN W A; SCHNEPS J; **WALD H B**
CS UNIV LONDON IMPERIAL COLL SCI & TECHNOL, LONDON SW7 2AZ, ENGLAND; RUTHERFORD APPLETON LAB, DIDCOT OX11 0QX, OXON, ENGLAND; CENS, F-91190 GIF SUR YVETTE, FRANCE; STANFORD UNIV, STANFORD LINEAR ACCELERATOR CTR, STANFORD, CA, 94305; TOHOKU UNIV, SENDAI, MIYAGI 980, JAPAN; TUFTS UNIV, MEDFORD, MA, 02155
CYA ENGLAND; FRANCE; USA; JAPAN
SO NUCLEAR PHYSICS B, (1984) Vol. 244, No. 2, pp. 277-312.
DT Article; Journal
FS PHYS
LA ENGLISH
REC Reference Count: 21

L60 ANSWER 37 OF 39 SCISEARCH COPYRIGHT 1998 ISI (R)
AN 83:138989 SCISEARCH
GA The Genuine Article (R) Number: QG046
TI EVIDENCE FOR A NARROW NNBAR STATE AT 2.02 GEV/C2 IN 6 AND 9 GEV/C ANTI-PROTON INTERACTIONS
AU AZOOZ F (Reprint); BUTTERWORTH I; DORNAN P J; HALL G; STERN R A; WHITE A P; BROWN R C; **BUTLER N**; GOPAL G P; MCPHERSON A; SEKULIN R L; BARLOUTAUD R; CAMBIER J L; LORET M; OKUSAWA T; STEVENS R; VILANOVA D; BRAU J E; CARROLL J T; CHALOUPKA V; CAUTIS C V; DUMONT J J; ERICSON R A; FIELD R C; FREYTAG D R; GRANDPEIX J Y; KITAGAKI T; TANAKA S; YUTA H; ABE K; HASEGAWA K; YAMAGUCHI A; TAMAI K; TAKANASHI H; MANN W A; SCHNEPS J; **WALD H B**
CS UNIV LONDON IMPERIAL COLL SCI & TECHNOL, LONDON SW7 2AZ, ENGLAND (Reprint); RUTHERFORD & APPLETON LAB, CHILTON OX11 0QX, OXON, ENGLAND; CENS, F-91190 GIF SUR YVETTE, FRANCE; STANFORD UNIV, STANFORD LINEAR ACCELERATOR CTR, STANFORD, CA, 94305; TOHOKU UNIV, SENDAI, MIYAGI 980, JAPAN; TUFTS UNIV, MEDFORD, MA, 02155
CYA ENGLAND; FRANCE; USA; JAPAN
SO PHYSICS LETTERS B, (1983) Vol. 122, No. 5-6, pp. 471-475.

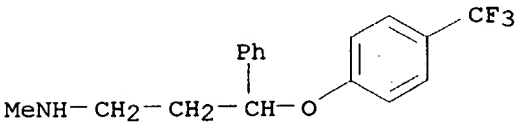
DT Article; Journal
FS PHYS
LA ENGLISH
REC Reference Count: 10

L60 ANSWER 38 OF 39 SCISEARCH COPYRIGHT 1998 ISI (R)
AN 83:343950 SCISEARCH
GA The Genuine Article (R) Number: QY516
TI CHARM PHOTOPRODUCTION CROSS-SECTION AT 20 GEV
AU ABE K (Reprint); BACON T C; BALLAM J; BERNY L; BEVAN A V; BINGHAM H H; BRAU J E; BRAUNE K; BRICK D; BUGG W M; **BUTLER J**; CAMERON W; CARROLL J T; CAUTIS C V; CHIMA J S; COHN H O; COLLEY D C; CONDO G T; DADO S; DIAMOND R; DORNAN P J; ERICKSON R; FIEGUTH T; FIELD R C; FORTNEY L; FRANEK B; FUJIWARA N; GEARHART R; GLANZMAN T; GOLDBERG J J; GOPAL G P; GOSHAW A T; HAFEN E S; HAGOPIAN V; HALL G; HANCOCK E R; HANDLER T; HARGIS H J; HART E L; HARIDAS P; HASEGAWA K; HAYASHINO T; HUANG D Q; HULSIZER R I; ISAACSON S; JOBES M; KALMUS G E; KELSEY D P; KENT J; KITAGAKI T; LANNUTTI J; LEVY A; LUCAS P W; MACDERMOTT M; MANN W A; MARUYAMA T; MERENYI R; MILBURN R; MILSTENE C; MOFFEIT K C; MURRAY J J; NAPIER A; NOGUCHI S; OCHIAI F; ONEALE S; PALOUNEK A P T; PLESS I A; RABIN M; RANKIN P; ROBERTSON W J; ROGERS A H; RONAT E; RUDNICKA H; SATO T; SCHNEPS J; SEWELL S J; SHANK J; SHAPIRO A M; SINCLAIR C K; SUGAHARA R; SUZUKI A; TAKAHASHI K; TAMAI K; TANAKA S; TETHER S; **WALD H B**; WALKER W D; WIDGOFF M; WILKINS C G; WOLBERS S; WOODS C A; WU Y; YAMAGUCHI A; YAMAMOTO R K; YAMASHITA S; YEKUTIELI G; YOSHIMURA Y; YOST G P; YUTA H
CS UNIV BIRMINGHAM, BIRMINGHAM B15 2TT, W MIDLANDS, ENGLAND (Reprint); BROWN UNIV, PROVIDENCE, RI, 02912; DUKE UNIV, DURHAM, NC, 27706; FLORIDA STATE UNIV, TALLAHASSEE, FL, 32306; UNIV LONDON IMPERIAL COLL SCI & TECHNOL, LONDON SW7 2BZ, ENGLAND; OAK RIDGE NATL LAB, OAK RIDGE, TN, 37830; RUTHERFORD & APPLETON LAB, DIDCOT OX11 0QX, OXON, ENGLAND; STANFORD UNIV, STANFORD LINEAR ACCELERATOR CTR, STANFORD, CA, 94305; TECHNION ISRAEL INST TECHNOL, IL-32000 HAIFA, ISRAEL; TOHOKU UNIV, SENDAI, MIYAGI 980, JAPAN; TUFTS UNIV, MEDFORD, MA, 02155; UNIV CALIF BERKELEY, BERKELEY, CA, 94720; TEL AVIV UNIV, TEL AVIV, ISRAEL; UNIV TENNESSEE, KNOXVILLE, TN, 37916; WEIZMANN INST SCI, IL-76100 REHOVOT, ISRAEL; NATL LAB HIGH ENERGY PHYS, TSUKUBA GUN, IBARAKI 305, JAPAN
CYA ENGLAND; USA; ISRAEL; JAPAN
SO PHYSICAL REVIEW LETTERS, (1983) Vol. 51, No. 3, pp. 156-159.
DT Article; Journal
FS PHYS
LA ENGLISH
REC Reference Count: 11

L60 ANSWER 39 OF 39 SCISEARCH COPYRIGHT 1998 ISI (R)
AN 82:258765 SCISEARCH
GA The Genuine Article (R) Number: NR327
TI LIFETIMES OF CHARMED PARTICLES PRODUCED IN A 20-GEV GAMMA-P

=> d l1 1 2

L1 ANSWER 1 OF 2 REGISTRY COPYRIGHT 1998 ACS
RN 56296-78-7 REGISTRY
CN Benzenepropanamine, N-methyl-.gamma.-[4-(trifluoromethyl)phenoxy]-, hydrochloride (9CI) (CA INDEX NAME)
OTHER NAMES:
CN (.+-.)-N-Methyl-3-phenyl-3-[4-(trifluoromethyl)phenoxy]propylamine hydrochloride
CN **Fluoxetine hydrochloride**
CN Lilly 110140
CN LY 110140
CN Prozac
DR 59333-67-4
MF C17 H18 F3 N O . Cl H
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CBNB, CIN, CSCHEM, DRUGPAT, EMBASE, HSDB*, IPA, MRCK*, NIOSHTIC, PHAR, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (54910-89-3)



● HCl

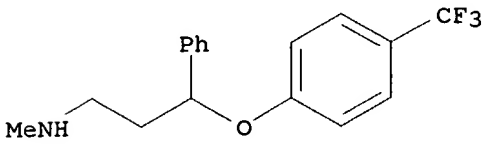
82 REFERENCES IN FILE CA (1967 TO DATE)
82 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 2 OF 2 REGISTRY COPYRIGHT 1998 ACS
RN 54910-89-3 REGISTRY
CN Benzenepropanamine, N-methyl-.gamma.-[4-(trifluoromethyl)phenoxy]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzenepropanamine, N-methyl-.gamma.-[4-(trifluoromethyl)phenoxy]-, (.+-.)-
OTHER NAMES:
CN (.+-.)-Fluoxetine
CN (.+-.)-N-Methyl-3-phenyl-3-[4-(trifluoromethyl)phenoxy]propylamine
CN dl-3-(p-Trifluoromethylphenoxy)-N-methyl-3-phenylpropylamine
CN **Fluoxetine**
DR 57226-07-0, 52341-67-0
MF C17 H18 F3 N O
CI COM

LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAPLUS, CASREACT, CEN, CHEMINFORMRX, CBNB, CIN, CSCHEM, CSNB, DDFU, DRUGNL, DRUGPAT, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL, VETU

(*File contains numerically searchable property data)

Other Sources: WHO



1292 REFERENCES IN FILE CA (1967 TO DATE)
14 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1299 REFERENCES IN FILE CAPLUS (1967 TO DATE)

EXPERIMENT

AU ABE K (Reprint); BACON T C; BALLAM J; BERNY L; BEVAN A V; BINGHAM H H; BRAU J E; BRICK D; BUGG W M; **BUTLER J**; CAMERON W; CARROLL J T; CAUTIS C V; CHIMA J S; COHN H O; COLLEY D C; CONDO G T; DADO S; DIAMOND R; DORNAN P J; ERICKSON R; FIEGUTH T; FIELD R C; FORTNEY L; FRANEK B; FUJIWARA N; GEARHART R; GOLDBERG J; GOPAL G P; GOSHAW A T; HAFEN E S; HAGOPIAN V; HALL G; HANCOCK E R; HANDLER T; HARGIS H J; HART E L; HARIDAS P; HASEGAWA K; HAYASHINO T; HUANG D Q; HULSIZER R I; ISAACSON S; JOBES M; KALMUS G E; KELSEY D P; KENT J; KITAGAKI T; LANG P; LANNUTTI J; LEVY A; LUCAS P W; MANN W A; MARUYAMA T; MACDERMOTT M; MERENYI R; MILBURN R; MILSTENE C; MOFFEIT K C; MURRAY J J; NAPIER A; NOGUCHI S; OCHIAI F; ONEALE S; PALOUNEK A P T; PLESS I A; RABIN M; RANKIN P; ROBERTSON W J; ROGERS A H; RONAT E; RUDNICKA H; SATO T; SCHNEPS J; SHANK J; SHAPIRO A M; SINCLAIR C; SUGAHARA R; SUZUKI A; TAKAHASHI K; TAMAI K; TANAKA S; TETHER S; **WALD H B**; WALKER W D; WIDGOFF M; WILKINS C G; WOLBERS S; WOODS C A; WU Y; YAMAGUCHI A; YAMAMOTO R K; YAMASHITA S; YEKUTIELI G; YOSHIMURA Y; YOST G P; YUTA H

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CYA ENGLAND; USA; JAPAN; ISRAEL

SO PHYSICAL REVIEW LETTERS, (1982) Vol. 48, No. 22, pp. 1526-1529.

DT Article; Journal

FS PHYS

LA ENGLISH

REC Reference Count: 19

FILE 'HOME' ENTERED AT 14:09:55 ON 15 DEC 1998